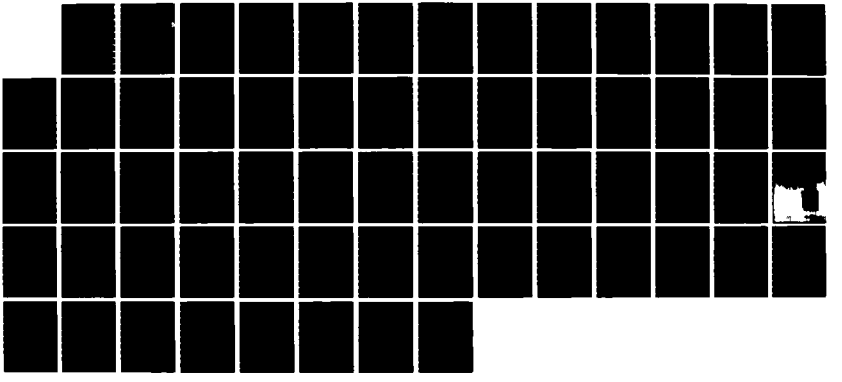
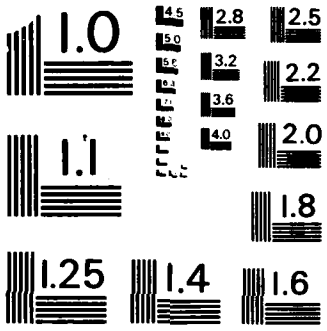
AD-A169 695 CONFERENCE ON THE NEUROBIOLOGY OF LEARNING AND MEMORY 1/1
(2ND)(U) CALIFORNIA UNIV IRVINE CENTER FOR THE
NEUROBIOLOGY OF LEARNING AND MEMOR J L MCGAUGH
UNCLASSIFIED 30 MAY 86 N00014-84-G-0108 F/G 5/10 NL





MICROCOPY RESOLUTION TEST CHART

NATIONAL BUREAU OF STANDARDS - 1963 - A

Unclassified

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION: Unclassified	1b. RESTRICTIVE MARKINGS
AD-A169 695	3. DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release; distribution unlimited
	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION: James L. McGaugh, University of Calif., Irvine (6b. OFFICE SYMBOL (If applicable))	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State and ZIP Code): Center for the Neurobiology of Learning & Memory, Irvine, CA 92714	7b. ADDRESS (City, State and ZIP Code)
8a. NAME OF FUNDING/SPONSORING ORGANIZATION: Office of Naval Research (8b. OFFICE SYMBOL (If applicable))	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER: Grant # N00014-84-G-0108
8c. ADDRESS (City, State and ZIP Code)	10. SOURCE OF FUNDING NOS.

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT NO.

11. TITLE (Include Security Classification): Second Conference on the Neurobiology of Learning and Memory

12. PERSONAL AUTHOR(S): McGaugh, James L.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Yr., Mo., Day)	15. PAGE COUNT
Final	FROM 07/01/84 TO 06/30/85	05/30/86	47

16. SUPPLEMENTARY NOTATION

17. COSATI CODES		
FIELD	GROUP	SUB. GR.

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number): Neurobiology, Memory

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Funds from this grant provided partial support for the Second Conference on the Neurobiology of Learning and Memory which was organized by the Center for the Neurobiology of Learning and Memory at the University of California, Irvine, and was held on October 6-9, 1984. The symposium focussed on three major topics: Brain systems and learning; Comparative aspects of learning and memory; and Learning, memory and cognitive processes. The program consisted of presentations by 18 major speakers and 53 poster presentations, and was attended by over 300 participants.

DTIC FILE COPY

DTIC ELECTE JUL 11 1986 S D

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS ☐	Unclassified

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE NUMBER (Include Area Code)	22c. OFFICE SYMBOL

DD FORM 1473, 83 APR — EDITION OF 1 JAN 73 IS OBSOLETE

SECURITY CLASSIFICATION OF THIS PAGE

SUMMARY REPORT

ONR GRANT N00014-84-G-0108

Funds from this grant provided partial support for the Second Conference on the Neurobiology of Learning and Memory which was organized by the Center for the Neurobiology of Learning and Memory at the University of California, Irvine. The Conference was held at the UC Irvine Campus and the Irvine Marriot Hotel on October 6-9, 1984. There were three major symposium sessions, three discussion sessions and a poster session. There was a total of 18 symposium and discussion speakers, 53 poster presentations and over 300 registered participants. Copies of the conference program and the poster abstracts are enclosed. A book based on the proceedings of the conference, Memory Systems of the Brain: Animal and Human Cognitive Processes (Norman M. Weinberger, James L. McGaugh, and Gary Lynch, Editors) was published (Guilford Press) in 1985. Three copies of the book were submitted to the Office of Naval Research at the time of publication. A copy of the book jacket is enclosed.

The symposium focussed on three major topics: Brain systems and learning; Comparative aspects of learning and memory; and Learning, memory and cognitive processes. The first, which concerned neural substrates of learning, addressed the nature of cellular mechanisms, loci of learning-induced plasticity within the nervous system, and long-term plasticity in a specific brain structure, the hippocampus. The presentations and discussions concerned plasticity in model systems as well as invertebrates and mammals. The evidence presented provides clear indication that progress is being made in achieving an understanding of cellular mechanisms of learning and memory.

The second topic, which concerned species differences in learning and memory, focussed on the question of whether species differences in learning reflect fundamental differences in neural organization. Extensive evidence of similar features of learning across species strongly argues for conserved mechanisms. However, the evidence of multiple forms of learning observed within and across species suggests that current psychological and neurobiological models of associative learning may be greatly oversimplified.

The third topic focussed on the question of whether learning and memory in humans is based on principles and neural systems common to those of infrahumans. The evidence reviewed strongly suggests that, in humans as well as animals, different forms of learning may be based on different neural systems. Considerable attention was given to the evidence that lesions of the medial temporal lobe impairs some forms of learning while sparing other forms.

A common theme of the Conference presentations and discussions is that learning comes in many forms and may be based on many neural systems. Such evidence greatly complicates efforts to achieve an understanding of the neural bases of learning and memory. But such evidence suggests that it is unwise to assume that matters are less complex. Subsequent research will need to confront directly the possibility that multiple mechanisms are required for the multiple forms of learning and memory.

Overall, the conference was highly useful in bringing these issues to focus in sessions involving many of the leading scientists investigating the neurobiological bases of learning and memory. The conclusions reached in the presentations and discussions provide strong direction for current research into the mechanisms of cognition.

These three reports should be processed as one report.
Per Dr. Donald P. Woodward, ONR/Code 1141NP

POSTER ABSTRACTS

Second Conference on the
Neurobiology of
Learning and Memory

University of California, Irvine
October 6 - 9, 1984

Poster Session: Monday, October 8
6:30 - 8:30 p.m.

Center for the Neurobiology of
Learning and Memory
University of California, Irvine

Posters presented by topic:

A - Long-term Potentiation
B - Synaptic Correlates of Plasticity
C - Learning and Memory: Electrophysiology
D - Learning and Memory: Pharmacology
E - Learning and Memory: Lesions
F - Learning and Memory: Behavior

Poster Session Chairs: Michel Baudry
Franz Hock
Frances Leslie

A - LONG-TERM POTENTIATION

A-1	MULTIPLE LONG-TERM EFFECTS OF PERFORANT PATH TETANIZATION ON INPUT/OUTPUT COUPLING IN THE DENTATE GYRUS	W.C. Abraham Dept. of Psychology Univ. of Otago Dunedin, New Zealand
A-2	VOLTAGE-CLAMP ANALYSIS OF LONG-TERM SYNAPTIC POTENTIATION	G. Barrionuevo, S. Kelso, T.H. Brown Division of Neurosciences Beckman Research Institute of the City of Hope Duarte, CA 91010
A-3	PHARMACOLOGICAL ANALYSIS OF NMDA RECEPTORS IN THE RAT BRAIN AND THEIR INVOLVEMENT IN POTENTIATION	E.W. Harris, D.T. Monaghan, A.H. Ganong, C.W. Cotman Dept. of Psychobiology Univ. of California Irvine, CA 92717
A-4	LONG TERM IMPAIRMENT OF LEARNING AND PYRAMIDAL CELL EXCITABILITY FOLLOWING THE INTRAHIPPOCAMPAL INJECTION OF TETANUS TOXIN IN RATS	J.G.R. Jefferys, H. Brace, J. Mellanby, S.F. Williams Sobell Dept. of Neurophysiology Inst. of Neurology London WC1N 3BG, England
A-5	TEMPORAL CONTIGUITY REQUIREMENTS FOR ASSOCIATIVE LONG-TERM POTENTIATION IN HIPPOCAMPAL SLICES	S.R. Kelso, T.H. Brown Div. of Neurosciences Beckman Research Institute of the City of Hope Duarte, CA 91010
A-6	PHYSIOLOGICAL PLASTICITY IN REPTILIAN CORTEX	J.R. Larson, G. Lynch Center for the Neurobiology of Learning and Memory Univ. of California Irvine, CA 92717
A-7	GABA SENSITIVITY DOES NOT CHANGE DURING LONG-TERM POTENTIATION IN RAT HIPPOCAMPAL SLICES	H.E. Scharfman, J.M. Sarvey Dept. of Pharmacology Uniformed Services University of the Health Sciences Bethesda, MD 20814
A-8	INHIBITION OF PROTEIN SYNTHESIS SPECIFICALLY BLOCKS NOREPINEPHRINE-INDUCED LONG-LASTING POTENTIATION IN THE FASCIA DENTATA OF RAT HIPPOCAMPAL SLICES	P.K. Stanton, J.M. Sarvey Dept. of Pharmacology Uniformed Services University of the Health Sciences Bethesda, MD 20814
A-9	DEPLETION OF NOREPINEPHRINE (NE), BUT NOT SEROTONIN (5-HT), SPECIFICALLY REDUCES LONG-TERM POTENTIATION (LTP) IN DENTATE OF RAT HIPPOCAMPAL SLICES	P.K. Stanton, J.M. Sarvey Dept. of Pharmacology Uniformed Services University of the Health Sciences Bethesda, MD 20814

B - SYNAPTIC CORRELATES OF PLASTICITY

B-1 THE INCORPORATION OF [^{35}S]-METHIONINE INTO CEREBRAL PROTEINS OF DIFFERENT BRAIN AREAS OF THE RAT DURING THE ACQUISITION AND AUTOMAINTENANCE OF AN INSTRUMENTAL TASK

V. Aleman, A. Oscos-Alvarado
Neurosciences Department
Centro de Investigacion y
de Estudios Avanzados del IPN
Apdo. Postal 14-740
Mexico, D.F. 07000

B-2 A FAMILY OF SYNAPTIC VESICLE-ASSOCIATED PHOSPHOPROTEINS: SYNAPSIN Ia, SYNAPSIN Ib, PROTEIN IIIa, and PROTEIN IIIb

M.D. Browning, P. Greengard
Lab. of Molecular & Cellular
Neuroscience
The Rockefeller University
New York, NY 10021

B-3 CHOLINERGIC REGULATION OF PROTEIN III PHOSPHORYLATION IN ISOLATED CHROMAFFIN CELLS

J.W. Haycock, M.D. Browning,
P. Greengard
Lab. of Molecular & Cellular
Neuroscience
The Rockefeller University
New York, NY 10021

B-4 A GOLGI-ELECTRON MICROSCOPIC STUDY OF MOSSY CELLS IN THE HIPPOCAMPAL DENTATE GYRUS

C.E. Ribak, L. Seress
Dept. of Anatomy
Univ. of California
Irvine, CA 92717

B-5 PHOSPHORYLATION IN THE CENTRAL NERVOUS SYSTEM OF LONG-TERM SENSITIZED APLYSIA

T. Saitoh
Howard Hughes Med. Inst. & the
Center for Neurobiol. & Behav.
Columbia University Col. P & S
New York, NY 10032

B-6 MORPHOLOGICAL CORRELATES OF PASSIVE AVOIDANCE TRAINING IN THE CHICK FOREBRAIN

M.G. Stewart
Brain Research Group
Dept. of Biology
The Open University
Milton Keynes, England MK7 6AA

C - LEARNING AND MEMORY: ELECTROPHYSIOLOGY

C-1	HIPPOCAMPAL NEURONS SHOW CONSISTENT PLACE FIELD ACTIVITY FOR EXTENDED PERIODS OF TIME IN A STABLE ENVIRONMENT	P.J. Best, L.T. Thompson Dept. of Psychology Univ. of Virginia Charlottesville, VA 22901
C-2	NORMAL LATENCY VARIABILITY IN THE AUDITORY EVENT-RELATED POTENTIAL	H.J. Michalewski, D. Prasher, A. Starr Dept. of Neurology Univ. of California Irvine, CA 92717
C-3	GENERATOR OF P300 IN THE CAT	T. O'Connor, A. Starr Dept. of Neurology Univ. of California Irvine, CA 92717
C-4	MONKEYS WITH LESIONS OF HIPPOCAMPUS AND AMYGDALA EXHIBIT EVENT-RELATED BRAIN POTENTIALS THAT RESEMBLE THE HUMAN P300 WAVE	K.A. Paller, S. Zola-Morgan, L.R. Squire, S.A. Hillyard Depts. of Neurosciences and Psychiatry Univ. of California, San Diego & VA Medical Center La Jolla, CA 92093
C-5	EVENT-RELATED POTENTIALS IN SQUIRREL MONKEYS EXHIBIT SIMILARITIES TO HUMAN SLOW POTENTIALS	J. Pineda, S. Foote, H. Neville Depts. of Neuroscience and Psychiatry Univ. of California, San Diego La Jolla, CA 92093
C-6	EVENT RELATED POTENTIALS TO SIMULTANEOUS AUDITORY AND VISUAL STIMULI	C.E. Rosenberg, L. Meyer, A. Starr Electrodiagnostic Lab. Univ. of California, Irvine Medical Center Orange, CA 92668
C-7	CAN SEPTAL TRANSPLANTS RESTORE SINGLE UNIT ACTIVITY IN THE HIPPOCAMPUS?	M.L. Shapiro, D. Simon, D.S. Olton Dept. of Psychology Johns Hopkins University Baltimore, MD 21218 F.H. Gage, A. Bjorklund, U. Stenevi Dept. of Histology Univ. of Lund Lund, Sweden
C-8	PLASTICITY OF FREQUENCY TUNING OF SINGLE NEURONS IN AUDITORY CORTEX DURING LEARNING	N.M. Weinberger, D.M. Diamond, T. McKenna Center for the Neurobiology of Learning and Memory Univ. of California Irvine, CA 92717

D - LEARNING AND MEMORY: PHARMACOLOGY

D-1	BRAIN BETA-ADRENERGIC MECHANISMS WOULD PARTICIPATE IN NALOXONE-INDUCED ENHANCEMENT OF MEMORY IN MICE	C.M.Baratti, I.B. Introini Catedra de Farmacologia Facultad de Farmacia y Bioquimica Universidad de Buenos Aires RA-1113, Buenos Aires, Argentina
D-2	EFFECTS OF THE CENTRAL BETA-ADRENOCEPTOR AGONIST CLENBUTEROL ON MEMORY CONSOLIDATION IN MICE	I.B. Introini, C.M. Baratti Catedra de Farmacologia Facultad de Farmacia y Bioquimica Universidad de Buenos Aires RA-1113, Buenos Aires, Argentina
D-3	AMPHETAMINE DISRUPTS BOTH WORKING AND REFERENCE MEMORIES OF RATS TRAINED IN A RADIAL MAZE	W.W. Beatty, R.A. Bierley, J.G. Boyd Dept. of Psychology North Dakota State Univ. Fargo, ND 58105
D-4	EPINEPHRINE FACILITATES INHIBITORY AVOIDANCE RETENTION OF ADRENAL DENERVATED RATS TREATED WITH A HIGH DOSE OF DSP4	C. Bennett, S. Kaleta, M. Arnold, J.L. McGaugh Center for the Neurobiology of Learning and Memory Univ. of California Irvine, CA 92717
D-5	MET-ENKEPHALIN: DIFFERENTIAL EFFECTS IN THE HIPPOCAMPUS	L. Cahill, H. Haigler, R. Kochman Searle Research & Development 4901 Searle Parkway Skokie, IL 60077
D-6	AMINO ACID AND GLUCOSE ENHANCEMENT OF MEMORY STORAGE: POSSIBLE MEDIATORS OF EPINEPHRINE EFFECTS ON MEMORY	P.E. Gold Dept. of Psychology Univ. of Virginia Charlottesville, VA 22901
D-7	LYSINE-VASOPRESSIN (LVP) ENHANCES RETENTION OF A SPATIAL DISCRIMINATION IN RATS	M.P. Hammer Dept. of Psychology Univ. of Alberta Edmonton, Alberta T6G 2E1, Canada
D-8	FUNCTIONAL ACTIVITY IN THE BRAIN OF SOCIALLY DEPRIVED RATS PRODUCED BY AN ACTIVE AVOIDANCE TEST AFTER HOE 175 AND CLOBAZAM TREATMENTS: A 2-DEOXYGLUCOSE STUDY	F.J. Hock, H. Scheich HOECHST AG P.O. Box 800320 D-6230 Frankfurt/ M.80 Federal Republic of Germany

D-9 EFFECTS OF PERIPHERAL EPINEPHRINE, 4-OH AMPHETAMINE, AND D-AMPHETAMINE ON THE MAINTAINED DISCHARGE OF CELLS IN THE LOCUS COERULEUS

R.N. Holdefer, R.A. Jensen
Dev. Biopsychology Laboratory
Southern Illinois Univ.
Carbondale, IL 62901

D-10 B-ENDORPHIN EFFECTS ON RETRIEVAL, AND THE NEURAL PATHWAYS INVOLVED IN THE BRAIN B-ENDORPHIN RELEASE CAUSED BY TRAINING

I. Izquierdo, C.A. Netto
Depto. Bioquimica
UFRGS
90000 Porto Alegre, Brazil

D-11 AMYGDALA NORADRENERGIC SYSTEM & MEMORY MODULATION: INVOLVEMENT IN THE ENHANCING EFFECT OF PERIPHERAL EPINEPHRINE

K.C. Liang, R.G. Juler, J.L. McGaugh
Center for the Neurobiology of Learning and Memory
Univ. of California
Irvine, CA 92717

D-12 DES-GLY VASOPRESSIN (DGAVP) FACILITATES ACQUISITION OF AUTOSHAPED OPERANT AND ADJUNCTIVE BEHAVIORS AT TWO LEVELS OF TASK DIFFICULTY

R.B. Messing, S.B. Sparber
Dept. of Pharmacology
Univ. of Minnesota
Minneapolis, MN 55455

D-13 FACILITATION OF RETRIEVAL FOLLOWING PRE-TEST ADMINISTRATION OF PIRENPERONE IN MICE

H.J. Normile, H.J. Altman
Lafayette Clinic
Detroit, MI 48207

D-14 ROLE OF ALPHA- AND BETA-ADRENERGIC RECEPTORS IN LEARNING AND MEMORY IN MICE

G.D. Novack, D.B. Sternberg, J.L. McGaugh
Center for the Neurobiology of Learning and Memory
Univ. of California
Irvine, CA 92717

D-15 AMNESIA PRODUCED BY ANISOMYCIN IN AN APPETITIVE TASK IS NOT DUE TO LEARNED AVERSION

T.A. Patterson, M.R. Rosenzweig E.L. Bennett
Dept. of Psychology
Univ. of California
Berkeley, CA 94720

D-16 PSYCHOPHARMACOLOGICAL DISSOCIATION OF MEMORY AND ATTENTION

D.M. Warburton, K. Wesnes
Dept. of Psychology
Univ. of Reading
Reading, United Kingdom, RG6 2A

E - LEARNING AND MEMORY: LESIONS

E-1 HABIT FORMATION IN INFANT RHESUS MONKEYS: SEX-DEPENDENT EFFECTS OF INFERIOR TEMPORAL LESIONS

J. Bachevalier, M. Mishkin
Lab. of Neuropsychology
National Institute of Mental Health
Bethesda, MD 20205

E-2 BEHAVIORAL AND NEUROCHEMICAL CHARACTERIZATION OF THE EFFECTS OF NUCLEUS BASALIS OF MEYNERT LESIONS IN RATS

R.F. Berman, R.D. Crosland, D.J. Jenden, H.J. Altman
Dept. of Psychology
Wayne State Univ.
Detroit, MI 48202 &
Dept. of Pharm. and BRI
University of California
Los Angeles, CA 90024 &
Lafayette Clinic
Detroit, MI 48207

E-3 THE AMYGDALOID INVOLVEMENT IN THE ACQUISITION OF TASTE POTENTIATED ODOR AVERSION LEARNING

F. Bermudez-Rattoni, C.V. Grijalva, J.Garcia
Mental Retardation Res. Ctr.
University of California
Los Angeles, CA 90024 &
Centro de Investigaciones en Fisiologia Celular, UNAM

E-4 PLASTICITY OF SUBSTANTIA NIGRA PROJECTIONS AND THEIR RELATIONSHIP TO BEHAVIOR

J.P. Huston, S. Morgan, H. Steiner
Institute of Psychology III
Univ. of Dusseldorf
4000 Dusseldorf
Federal Republic of Germany

E-5 PASSIVE AVOIDANCE LEARNING AND MEMORY STORAGE IN DECEREBRATE RATS

C. Tomaz, J.P. Huston
Institute of Psychology III
Univ. of Dusseldorf
4000 Dusseldorf
Federal Republic of Germany

E-6 INTERRUPTION OF PROJECTIONS FROM THE MEDIAL GENICULATE NUCLEUS TO AN ARCHI-NEOSTRIATAL FIELD DISRUPTS AUDITORY FEAR CONDITIONING

J.E. LeDoux, A. Sakaguchi, J. Iwata, D.J. Reis
Lab. of Neurobiology
Cornell Univ. Med. Coll.
New York, New York 10021

E-7 DISSOCIATION OF NEURAL REGIONS NECESSARY FOR ALPHA AND CONDITIONED RESPONSES TO A VISUAL STIMULUS

R.W. Skelton, M.D. Mauk, R.F. Thompson
Dept. of Psychology
Stanford University
Stanford, CA 94305

F - LEARNING AND MEMORY: BEHAVIOR

F-1	DEVELOPMENT OF THE NEURAL NETWORK CONTROLLING SONG BEHAVIOR IN ZEBRA FINCHES	S.W. Bottjer, S.L. Glaessner, A.P. Arnold Dept. of Psychology Univ. of California Los Angeles, CA 90024
F-2	METABOLIC CORRELATES OF KINDLING-INDUCED CHANGES IN THE REWARDING EFFICACY OF HIPPOCAMPAL STIMULATION: A 2-DEOXYGLUCOSE AUTORADIOGRAPHIC STUDY	K.A. Campbell Dept. of Psychology Univ. of Pennsylvania Philadelphia, PA 19104
F-3	THE ENHANCED NEURAL RESPONSE INDUCED BY POSTNATAL OLFACTORY EXPERIENCE IN NORWAY RATS IS ODOR-SPECIFIC	R.M. Coopersmith, M. Leon Dept. of Psychobiology University of California Irvine, CA 92717
F-4	AGE DIFFERENCES IN PERFORMANCE OF RATS AND MICE IN A 14-UNIT T-MAZE	D. Ingram, E. Spangler, J. Freeman, W. Richards Gerontology Research Ctr. NIA, NIH Baltimore City Hospitals Baltimore, MD 21224
F-5	ONTOGENY AND PLASTICITY OF EXPLORATORY BEHAVIOR AND HIPPOCAMPAL DEVELOPMENT IN RATS	E.M. Kurz, B.L. Harkins, L. Nadel Program in Cognitive Sciences Univ. of California Irvine, CA 92717
F-6	FOOD STORAGE AND SPATIAL MEMORY IN CHICKADEES AND TITS	D.F. Sherry Dept. of Psychology Univ. of Toronto Toronto, Ontario, Canada M5S 1A
F-7	OLFACTORY LEARNING IN RATS AS A MODEL FOR STUDYING MEMORY IN COMBINATORIAL CIRCUITRIES	U. Staubli, D. Fraser, G. Lynch Center for the Neurobiology of Learning and Memory Univ. of California Irvine, CA 92717

A-1

MULTIPLE LONG-TERM EFFECTS OF PERFORANT PATH TETANIZATION ON INPUT/OUTPUT COUPLING IN THE DENTATE GYRUS. W.C. Abraham. Dept. Psychology, Univ. Otago, Dunedin, New Zealand.

Long-term potentiation of transmission at perforant path-granule cell synapses is accompanied by an increase in the size of the extracellularly recorded population spike (S) for a given population EPSP (E). This phenomenon has been termed E-S potentiation. As one step in determining whether long-term potentiation and E-S potentiation are related mechanistically, we investigated whether they emerged with different thresholds when given a series of increasingly intense tetani in rats anesthetized with sodium pentobarbital.

Single wire recording and stimulating electrodes were placed in the dentate hilus and the medial perforant path, respectively. Standard field potential recording techniques were used. High-frequency stimulation consisted of a series of 2-10 trains of constant frequency (250 Hz) and pulse intensity (100-500 μA, 250 μs) spaced 5-10 min apart. Trains within a series typically were of increasing duration. Input/output relations were determined before and at least 10 min after conditioning by delivering test stimuli of constant amplitude but varying in half-wave duration (10-250 μs). EPSP potentiation was measured as the change in slope of the function relating population EPSP slope to log stimulus intensity. The E-S amplitude curve was defined by the linear regression of the function relating spike amplitude to EPSP slope. The E-S latency curve was defined by the linear regression of the function relating spike onset latency to EPSP slope.

Long-term potentiation resulted from each series of trains and was positively correlated with the longest train in the series ($r=0.75$, $n=15$). However, the spike/EPSP relation changed in a complex manner, exhibiting a decrease in slope (E-S depression) but a shift to the left (E-S potentiation) of the E-S amplitude curve. For a given animal the three phenomena could be shown to appear at different train durations, with long-term potentiation having the lowest threshold and E-S potentiation having the highest. Furthermore, the three alterations typically reached asymptote at different train durations as well. A downward shift in the E-S latency curve was loosely related to the left-shift of the E-S amplitude curve and thus appeared to be another manifestation of E-S potentiation. The data confirm that dentate input/output coupling is altered by high-frequency perforant path activity in multiple ways and suggest that each may involve a different mechanism.

Funded by a New Zealand MRC grant to Prof. G.V. Goddard and an NIMH postdoctoral fellowship to W.C. Abraham.

A-2

VOLTAGE-CLAMP ANALYSIS OF LONG-TERM SYNAPTIC POTENTIATION. German Barrionuevo, Stephen Kelso and Thomas H. Brown. Division of Neurosciences, Beckman Research Institute of the City of Hope, Duarte, CA 91010.

Long-term synaptic potentiation (LTP) is an extremely persistent enhanced synaptic efficacy that can be induced by repetitive synaptic stimulation for periods of a few seconds or less.

The present investigation was conducted to examine the biophysical mechanisms underlying LTP in an identifiable and isolated monosynaptic input to hippocampal neurons. The results provide the first description of changes in the measured excitatory synaptic currents and conductances that accompany LTP. Intracellular recordings were made, using a time-share single microelectrode current- and voltage-clamp device, from pyramidal neurons region CA3 and sometimes region CA1. The slices were bathed in 10 μM picrotoxin to block the recurrent or feedforward inhibition that normally accompanies the monosynaptic excitatory synaptic inputs to these cells. LTP was induced by stimulating the afferents at 100 Hz for 1 sec. This tetanic stimulation was presented 2-4 times at 5 sec intervals.

Current-clamp analysis was used to assess the input resistance and the membrane time constant of the neurons before and after the induction of LTP. Voltage-clamp techniques were used to analyze the bipohysical changes produced by LTP. The peak synaptic current amplitude was measured as a function of the membrane holding potential. From this current-voltage relationship, the synaptically-induced conductance change and its reversal potential were measured before and after the induction of LTP.

LTP was observed in 22 CA3 and 4 CA1 pyramidal cells. The current-clamp experiments indicated that the increased synaptic efficacy observed during LTP was not accompanied by significant changes in the postsynaptic passive membrane properties, measured in the hyperolarizing direction. The voltage-clamp experiments demonstrated an increase in the measured peak synaptic currents, a corresponding increase in the measured peak synaptic conductance, but no change in the synaptic reversal potential. The latter finding demonstrates that LTP is not due to a change in the ionic selectivity property of the postsynaptic receptors. The results also demonstrate that the inhibitory component of the usual mixed synaptic response is not necessary for the induction of LTP.

(NIH Grants NS18861, NS18295 and a McKnight Foundation Scholar's Award.)

Pharmacological analysis of NMDA Receptors in the Rat Brain and their involvement in Potentiation. E.W. Harris, D.T. Monaghan, A.H. Ganong and C.W. Cotman, Dept. Psychobiology, University of California, Irvine CA 92717.

Receptors for acidic amino acids appear throughout the CNS and probably mediate neurotransmission at many excitatory synapses in the mammalian CNS. The best characterized of these receptors are preferentially activated by N-methyl-D-aspartate (NMDA). Little is known about the anatomical distribution of this class of receptors, and their involvement in synaptic transmission is also unclear since NMDA antagonists are not potent blockers at any identified monosynaptic pathway. Radioligand autoradiography has revealed that NMDA-sensitive ^{3}H-glutamate binding sites are especially numerous in strata radiatum and oriens of hippocampal area CA1. We have compared NMDA-displaceable binding, NMDA-evoked depolarizations, and long-term potentiation (LTP) of synaptic responses in stratum radiatum of rat hippocampal slices using a series of -phophono acidic amino acid analogs with a characteristic spectrum of antagonism of NMDA.

NMDA binding sites were demonstrated by quantitative autoradiography as previously described (Nature, 1983,306:176). NMDA-displaceable ^{3}H-glutamate binding was reduced by greater than 80% by 100uM ±AP5 (2-amino-5-phosphonopentanoate) or ±AP7 (2-amino-7-phosphonoheptanoate), but less than 30% by ±AP4 (2-amino-4-phosphonobutyrate) or ±AP8 (2-amino-8-phosphonooctanoate). ±AP6 (2-amino-6-phosphonohexanoate) was of intermediate potency.

Focal depolarizations produced by ionophoretic application of NMDA were reduced by bath application of 10uM -AP5 or +AP7 68%(± 2) and 44%(± 2) respectively. Application of 100uM ±AP4 +AP6 or ±AP8 reduced NMDA responses less than 20%. None of these treatments significantly reduced depolarizations produced by application of kainate or quisqualate.

LTP of extracellular synaptic responses in stratum radiatum (Schaffer collateral pathway) was produced by high frequency stimulation (100Hz, 1 second, three times). Addition of 50uM -AP5 or +AP7 had no effect on control synaptic potentials, but completely blocked LTP of both the synaptic response and the population spike. LTP could be induced once either drug was washed out, however. Addition of 100uM +AP5, ±AP4, ±AP6 or ±AP8 had no effect on control synaptic potentials or the development of LTP.

NMDA receptors examined in the hippocampus are pharmacologically similar to those described in spinal cord. NMDA binding is also enriched in synaptic membranes prepared from whole rat brain. Synaptic potentials probably do not result from activation of NMDA receptors, but these sites are involved in LTP. (Supported by DAMD 17-83-C-3189 & DAAG 29-82-K-0194).

LONG TERM IMPAIRMENT OF LEARNING AND PYRAMIDAL CELL EXCITABILITY FOLLOWING THE INTRAHIPPOCAMPAL INJECTION OF TETANUS TOXIN IN RATS.

John G.R.Jefferys, Helen Brace, Jane Mellanby & Sarah F.Williams, Sobell Dept.of Neurophysiology, Inst.of Neurology, Queen Square, London WC1N 3BG (JJ & SW), and Dept. of Experimental Psychology, Oxford Univ., Oxford OX1 3UD (HB & JM), England.

Learning and memory are impaired for many months after remission from the spontaneous generalized seizures which occur for a few weeks following intrahippocampal injection of tetanus toxin (2-12 mouse LD50) (Mellanby et al, 1982, Expl Neurol. 75, 690-699). We have examined the behavioural deficit using 2 learning tasks in which the hippocampus has been implicated: the radial arm maze (Olton et al, 1979, Behav.Brain Sci. 2, 313-365) where the rat has to locate food rewards on each of the 8 arms; and the circular platform task (Barnes, 1979, J. comp. physiol. Psychol. 93,74-104) where the rat has to locate the 1 hole (of 18) leading to a dark tunnel to escape from bright illumination. Toxin injected rats learnt both tasks more slowly than control injected.

3-6 months after injection, we examined the physiological function of hippocampal pyramidal cells in a terminal acute experiment under 1% halothane. Long term potentiation could be induced in the commissural (comm) input to CA3 pyramidal cells, and lasted up to 6h., even in the rats with the greatest learning impairment. However, comm and mossy fibre postsynaptic population spikes were smaller in the toxin group (appx. halved on average, and almost absent in some rats); no loss of afferents or of pyramidal cells was apparent as population e.p.s.p.s and antidromic population spikes were unaffected. This reduction in excitability (?increased inhibition) in CA3 was less marked remote from the site of toxin injection, was not found in CA1, and was reversed following LTP. We propose that the inhibition of CA3 responsiveness may be involved in the remission from the epileptic syndrome and in the subsequent learning impairment.

Supported by the Thorn Trust, M.R.C. and Ciba Geigy

TEMPORAL CONTIGUITY REQUIREMENTS FOR ASSOCIATIVE LONG-TERM POTENTIATION IN HIPPOCAMPAL SLICES. S. R. Kelso and T. H. Brown, Div. of Neurosciences, Beckman Research Institute of the City of Hope, Duarte, CA 91010.

Associative long-term potentiation (LTP) has been suggested as a possible mechanism for aspects of learning and memory. In the in vitro hippocampal slice preparation, a conditioning stimulus train delivered to a weak synaptic input to the CA1 region produced LTP in that pathway only if a separate stronger input to this region was concurrently stimulated with a conditioning train (Barrionuevo & Brown, Proc. Natl. Acad. Sci. 80:7347, 1983). This phenomenon was termed associative rather than heterosynaptic LTP because presenting the same conditioning train to the strong input alone did not produce LTP in the weak input.

We were interested in the timing rules governing the induction of associative LTP. To what extent do the temporal contiguity requirements resemble those observed behaviorally in classical conditioning studies? Can associative LTP be induced if the conditioning trains that are presented to the two pathways are separated in time? More generally, how does the interstimulus interval affect the occurrence, magnitude and duration of associative LTP? Such information is relevant to the possible role of associative LTP in learning and memory and also to the design of experiments aimed at understanding the biophysical and biochemical mechanisms responsible for this intriguing phenomenon.

We have begun to investigate formal analogs to forward, backward, and delay classical conditioning. Before and 20 min after presenting a 100 Hz conditioning train to the two synaptic inputs to the CA1 region, the amplitude of the response to the weak input was tested every 6 seconds. The conditioning trains presented to the weak and strong inputs lasted 600 and 400 msec, respectively. In the forward conditioning paradigm, the onset of the weak-input conditioning train preceded the onset of the strong-input conditioning train by 200 msec. In the backward paradigm, the onset of the train delivered to the strong input preceded the weak-input train by 750 msec. In the delay conditioning paradigm, the onset of the train delivered to the weak input preceded the strong-input train by 600 msec.

Our preliminary results indicate that only the forward conditioning paradigm is effective in inducing associative LTP. Supported by NIH grant NS07408, AFOSR Contract F49620 and a McKnight Foundation Scholar's Award.

PHYSIOLOGICAL PLASTICITY IN REPTILIAN CORTEX. J.R. Larson and G. Lynch. Center for the Neurobiology of Learning and Memory, Univ. Calif., Irvine, CA 92717.

Long-term potentiation (LTP) of excitatory postsynaptic potentials occurs in several mammalian forebrain pathways after brief periods of high frequency synaptic activity. It is not known to what extent the brains of nonmammalian vertebrates possess this remarkable form of synaptic plasticity. We now report that high frequency stimulation of a cortical pathway in a reptile results in a long-lasting enhancement of synaptic responses which resembles LTP found in mammalian brain.

Lizard cerebral cortex consists of four longitudinally arrayed sheets of cells - the medial, dorsomedial, dorsal, and lateral cortical fields. The lateral ventricle separates most of the cortex from the rest of the forebrain; thus it is possible to isolate the entire cortex with minimal damage by making cuts at its medial and lateral boundaries. The resulting thin slab of tissue can be removed and maintained in vitro for extended periods (>12 hr). This preparation retains the advantageous features of mammalian brain slices for electrophysiological experiments while reducing the relative amount of tissue damaged by slicing.

Experiments were performed on mature male desert iguanas (Dipsosaurus dorsalis). Stimulation of dorsal or lateral cortex evoked a large short-latency negative potential recorded at the pial surface of medial cortex. Neuronal somata in this field are concentrated in a single layer with basal and apical dendrites radiating in relatively cell-free laminae to the ventricular and pial surfaces. Laminar profile analysis revealed that the evoked field potential was localized to the apical dendritic zone of medial cortex neurons; this zone is the termination site of afferents from lateral and dorsal cortex (Lohman & Mentink, Brain Res., 45:325, 1972). These results suggest that the response reflects inward current associated with dendritic EPSPs.

In eight of ten preparations studied, high frequency stimulation (100 Hz for .5-1 sec) resulted in a facilitation of the response lasting the duration of a twenty minute test period. This potentiation can persist for at least three hours, the longest interval tested. Experiments with two stimulation electrodes spaced widely in the rostral-caudal dimension suggested that when two sets of afferents to the same population of postsynaptic cells were tested, high frequency stimulation of one set resulted in potentiation specific to that set.

These experiments indicate that reptilian cortex possesses a form of plasticity similar to LTP seen in mammalian hippocampus. The in vitro preparation of reptilian cortex described here will permit more complete characterization of this phenomenon.

GABA SENSITIVITY DOES NOT CHANGE DURING LONG-TERM POTENTIATION IN RAT HIPPOCAMPAL SLICES. H. E. Scharfman and J. M. Sarvey, Department of Pharmacology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814

Long-term potentiation (LTP) in the hippocampus is a long-lasting enhancement of synaptic efficacy, following high frequency, repetitive stimulation. Changes in excitatory or inhibitory pathways may mediate LTP. Evidence that the IPSP decreases in amplitude during LTP suggests that an alteration of inhibitory processes could be important to the production of LTP. We asked whether a decrease in postsynaptic sensitivity to the major inhibitory transmitter in the hippocampus, gamma-aminobutyric acid (GABA), could explain the depression of the IPSP during LTP.

Extracellular recordings were taken from the CA1 cell body layer of 375um hippocampal slices. Stimulation of the stratum radiatum was used to produce a population spike. GABA (10mM) was pressure-ejected through a micropipette placed within 50um of the recording electrode. Postsynaptic sensitivity to GABA was tested at the soma, since the IPSP is thought to be produced by somatic GABA receptors. GABA produced a dose-dependent, reversible inhibition of the population spike amplitude, without affecting the extracellularly recorded EPSP. A fixed amount of GABA inhibited the same percentage of the population spike, with a similar time course of recovery, regardless of the amplitude of the spike. In some cases, the short period of inhibition was immediately followed by an equally short period when the population spike showed a rebound increase in amplitude, and then returned to control amplitude.

In most experiments, repetitive stimulation (100 Hz for 2 sec) produced short-term potentiation of the population spike (STP; 1-15 min duration; mean % of control amplitude ± SEM : 202% ± 35.0) followed by LTP (duration $\geq$ 1 hr; 209% ± 17.0). Neither the inhibition, duration of effect, dose-dependence, nor rebound (when it occurred) changed after repetitive stimulation, whether STP and LTP occurred or not (n=12). Preliminary evidence suggests that the same is true in field CA3 (n=2) and the fascia dentata (n=2). This suggests that a decrease in postsynaptic sensitivity to GABA is not the mechanism for the depression of the IPSP which occurs during LTP. A decrease in transmitter release may be an alternative explanation.

INHIBITION OF PROTEIN SYNTHESIS SPECIFICALLY BLOCKS NOREPINEPHRINE-INDUCED LONG-LASTING POTENTIATION IN THE FASCIA DENTATA OF RAT HIPPOCAMPAL SLICES. P.K. Stanton and J.M. Sarvey. Dept. of Pharmacology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814.

Hippocampal long-term potentiation (LTP) is a long-lasting enhancement in synaptic efficacy after brief, high frequency repetitive stimulation. We have provided evidence that ongoing protein synthesis is required for LTP to occur. Other groups have shown that depletion of forebrain norepinephrine (NE) by 6-hydroxydopamine reduces the amplitude of LTP in the fascia dentata, and NE potentiates the evoked population response in the same area. Our study was undertaken to better characterize the NE-induced potentiation in the fascia dentata, and to test the ability of the protein synthesis inhibitor emetine to block this potentiation as it does LTP.

Extracellular potentials evoked in the dentate by stimulating the perforant path were recorded in hippocampal slices (400um thick). NE was bath perfused for 30 min at 1,5, 10,50 or 100 µM. The increase in spike amplitude after 30 min of NE perfusion was defined as NE-induced potentiation (NEP), and potentiation after an additional 30 min drug-free wash was defined as NE-induced long-lasting potentiation (NELLP). NE produced a dose-dependent potentiation of the population spike during the 30 min perfusion, which increased after the 30 min wash (% of control ± SEM; * p<.05, paired t-test).

[NE] (µM)	N	30 min NE (NEP)	30 min WASH (NELLP)
1	4	108.9 ± 4.6	105.0 ± 15.4
5	4	99.6 ± 12.9	122.0 ± 22.2
10	8	143.7 ± 13.4*	149.8 ± 19.9*
50	7	146.2 ± 13.1*	164.6 ± 27.8*
100	6	140.8 ± 11.0*	178.2 ± 25.2*

Both NEP and NELLP were completely antagonized by the ß antagonist propranolol (50µM,N=4), and were specific to the fascia dentata, since NE (50µM,N=3) produced only a slight, transient depression in spike amplitude in field CA1. The protein synthesis inhibitor emetine (15µM, which inhibits protein synthesis in slices by >95%) perfused for 30 min before, and throughout the NE perfusion (50µM) and wash, did not alter the NEP seen during perfusion of NE (146.0 ± 21.8%, N=6), but blocked NELLP after the wash (113.1 ± 3.8%,N=6).

These results parallel blockade of LTP by protein synthesis inhibitors, and suggest a necessity for newly synthesized or rapidly turned over proteins in the production of NELLP.

DEPLETION OF NOREPINEPHRINE (NE), BUT NOT SEROTONIN (5-HT), SPECIFICALLY REDUCES LONG-TERM POTENTIATION (LTP) IN DENTATE OF RAT HIPPOCAMPAL SLICES. P.K. Stanton and J.M. Sarvey, Dept. of Pharmacology, Uniformed Services University of the Health Sciences, Bethesda, MD 20814.

In vivo studies have shown that depletion of NE by 6-hydroxydopamine (6-OHDA),or of 5-HT by 5,7-dihydroxytryptamine (5,7-DHT) or p-chlorophenylalanine (PCPA),reduces LTP in the dentate. However, one cannot tell whether this resulted from depletion in the hippocampus itself, or other brain areas, and there was no comparison between hippocampal fields. Rats were depleted of NE by 6-OHDA (6ug bilateral,dorsal noradrenergic bundle), or of 5-HT by 5,7-DHT (300ug,lateral ventricle) or PCPA (2x200mg/kg, i.p.). After a 14 (6-OHDA;5,7-DHT) or 2 (PCPA) day delay to maximally deplete, slices were cut. Control LTP occurrence was 47% in dentate (14 of 31); 57% in CA1 (16 of 28). Depletion of NE reduced LTP occurrence in dentate to 17% (χ^2,$p<.05$,4 of 24), but did not reduce LTP in CA1 (89%,9 of 11). In contrast, depletion of 5-HT had no effect on LTP either in dentate (45%, 13 of 29), or in CA1 (60%,6 of 10). Hippocampal depletion in separate rats was: 6-OHDA=↓79.4 $\pm$ 6.5%;5,7-DHT=↓65.8 $\pm$ 8.6%;PCPA=↓76.7 $\pm$ 1.2%. The data suggest endogenous hippocampal NE, specifically in dentate, is more important to LTP than is endogenous 5-HT.

THE INCORPORATION OF [^{35}S]-METHIONINE INTO CEREBRAL PROTEINS OF DIFFERENT BRAIN AREAS OF THE RAT DURING THE ACQUISITION AND AUTOMAINTENANCE OF AN INSTRUMENTAL TASK. V. Alemán and A. Oscós-Alvarado.Neurociences Department, Centro de Investigación y de Estudios Avanzados del IPN, Apdo. Postal 14-740, México, D.F. 07000.

During learning acquisition,animals initiate, improve, and increase the responding rate until a maximum efficiency. During automaintenance (overtraining) animals sustain their high responding efficiency as long as they are interacting with the learned contingencies. These two different stages of learning may result from two different physiological and molecular processes. Thus it seemed of interest to study protein metabolic changes in the brain during automaintenance. Three different groups (n=6) of Wistar-Porton 90-day old female rats were used: passive control, acquisition of autoshaping, and automaintenance groups. The training procedure consisted of the paired presentation of a conditioned stimulus (illumination for 10 seconds of a plexiglass lever) and the unconditioned stimulus (a 45 mg food pellet) and an intertrial interval of 70 seconds. The acquisition group was trained for three days and the maintenance group for 19 days (3 and 19 sessions), Except for the first (10 trials), each of the following sessions consisted of 50 trials. Fifteen minutes before the last three sessions animals received [^{35}S]-methionine injections (1.0μCi/g of body weight). In automaintained animals the degree of labeled amino acid incorporated into proteins of the cytoplasmic fraction from caudate, amygdala, hippocampus and temporo-parietal cortex was statistically lower ($p<0.01$) as compare to passive control rats. In the same automaintained animals the incorporation into synaptosomal proteins from both amygdala and hippocampus decreased in a statistically significant manner ($p\leq0.05$), but no in the other two brain areas. In a different experiment,and by means of an analysis of variance, the degree of label incorporated into proteins of cytoplasmic fractions from passive control, acquisition and automaintained groups were compared. In the latter group we found a significant decrease in incorporation ($p\leq0.06$) in all areas studied (caudate, hippocampus, and frontal cortex) as compared to the other groups. On the other hand a significant increase in incorporation was found in the acquisition group as compared to other groups ($p\leq0.06$). However in the synaptosomal fraction (P_2) of the acquisition group we found a non-significant decrease of incorporation in all brain areas analyzed, as compared to passive control group. On the other hand we found a significant decrease ($p\leq0.6$) in the degree of label incorporated in all brain areas of the automaintained group as compared to the passive control.

A FAMILY OF SYNAPTIC VESICLE-ASSOCIATED PHOSPHOPROTEINS: SYNAPSIN Ia, SYNAPSIN Ib, PROTEIN IIIa, AND PROTEIN IIIb. M.D. Browning and P. Greengard. Laboratory of Molecular and Cellular Neuroscience, The Rockefeller University, New York, N.Y. 10021.

Previous studies from our laboratory have shown that there are four prominent phosphoproteins present in acid extracts from all regions of the central nervous system (Synapsin Ia, M_r 85,000; Synapsin Ib, M_r 80,000; Protein IIIa, M_r 74,000; and Protein IIIb, M_r 55,000). All four of these proteins are phosphorylated in intact nerve cells by electrical stimulation in the presence of calcium, by depolarization in the presence of calcium, and by 8-bromo cAMP. We now report that these four phosphoproteins appear quite homologous. When the proteins were phosphorylated by cAMP-dependent protein kinase and then subjected to limit digestion by trypsin and chymotrypsin, only a single phosphopeptide was obtained from each protein; and these four phosphopeptides very nearly comigrate on 2-dimensional peptide maps. A number of monoclonal and serum antibodies raised against Protein III exhibit significant cross-reactivity toward Synapsin I. Quantitative immunolabeling in SDS-polyacrylamide gels was used to determine the concentration of these proteins in a variety of tissues, brain regions and subcellular fractions. The proteins were, with one exception, found only in nervous tissue; and, in the central nervous system, all four proteins exhibited a distribution that paralleled the relative density of nerve terminals in the region studied. The single exception to the exclusively neuronal distribution of these proteins is that Protein III has been found in the adrenal medulla. The subcellular distribution of the four proteins in brain tissue was also essentially identical since all four proteins were substantially enriched only in the synaptic vesicle fraction

These data indicate that four prominent phosphoproteins which are phosphorylated in parallel in intact nerve cells possess significant structural homology and are co-localized within the presynaptic terminal in association with synaptic vesicles. These data suggest that these proteins constitute a family of phosphoproteins that have similar roles in brain presumably mediating or modulating some aspect of synaptic vesicle function.

CHOLINERGIC REGULATION OF PROTEIN III PHOSPHORYLATION IN ISOLATED CHROMAFFIN CELLS. J.W. Haycock, M.D. Browning and P. Greengard. Lab. Molecular and Cellular Neuroscience, The Rockefeller University, New York, NY 10021.

A family of synaptic vesicle-associated phosphoproteins (Synapsin Ia and Ib, Protein IIIa and IIIb) exists in central and peripheral neurons. Suspension cultures of adrenal medullary chromaffin cells do not have detectable levels of Synapsin Ia and Ib but do contain both Protein IIIa and Protein IIIb (referred to collectively as Protein III). As measured both by immunolabeling of SDS-PAGE slab gels and by a detergent-based RIA, the levels of Protein III are 5-10% of those found in brain.

Treatments which activate stimulus-secretion coupling processes increase the phosphorylation state of both Synapsin I and Protein III in several tissue preparations (brain slices, posterior pituitary explants, and superior cervical ganglion explants). In the present studies we have investigated the regulation by acetylcholine (ACh) of Protein III phosphorylation in chromaffin cells isolated from bovine adrenal medulla.

Incubation of chromaffin cell monolayers with $^{32}PO_4$ led to a time-dependent ^{32}P-incorporation into several protein bands revealed by SDS-PAGE. Addition of polyvalent serum anti-Protein III antibodies to SDS extracts of the chromaffin cells immunoprecipitated both an Mr=74,000 (Protein IIIa) and an Mr=58,000 (Protein IIIb) phosphoprotein band. Partial proteolysis of phosphorylated Protein IIIa and IIIb, cut from the SDS-PAGE gels, with S. aureus V8 produced an Mr=18,000 phosphopeptide fragment (characteristic of Protein III from brain) from each band. The incorporation of ^{32}P into Protein IIIa and IIIb was time-dependent, and addition of ACh produced a rapid, 2-4 fold increase in ^{32}P incorporation into each of these bands. This increase was maintained for several minutes and was completely dependent upon extracellular calcium. Parallel experiments investigating the ACh-induced release of previously accumulated ^3H-norepinephrine yielded similar results.

The identities of the second messenger(s) and protein kinase(s) responsible for the ACh-induced phosphorylation of Protein III and the role which this phosphorylation may play in the ACh-induced release of ^3H-norepinephrine are under investigation.

A GOLGI-ELECTRON MICROSCOPIC STUDY OF MOSSY CELLS IN THE HIPPOCAMPAL DENTATE GYRUS. C.E. Ribak and L. Seress. Dept. of Anatomy, Univ. of Calif., Irvine, CA 92717.

The mossy cell is the most frequent cell type in the hilus of the hippocampal dentate gyrus and is distinguished from other neurons by the many "thorny excrescences" located on its soma and dendrites. These excrescences or large complex spines are characteristic for dendrites postsynaptic to mossy fibers because CA3 pyramidal cells display similar large spines on a restricted region of their proximal dendrites where mossy fibers are found. Previous studies of the dentate gyrus have not described the ultrastructural features and connections of the mossy cells. In the present study, a combined Golgi-electron microscopic method was used to identify these cells and retrograde HRP methods were used to determine if mossy cells have commissural projections. The mossy cells identified in our light microscopic preparations have: 1) an extensive dendritic arborization restricted to the hilus, 2) numerous thorny excrescences on their somata and dendrites 3) triangular or multipolar shaped somata and 4) axons that are directed toward the hippocampus with a few local collaterals. In electron microscopic preparations, the somata display round nuclei that lack infoldings and intranuclear rods. The perikaryal cytoplasm contains the typical organelles found in pyramidal cells. However, the mossy cell bodies display numerous somal spines and some of them have complex shapes and branching patterns. Three to four large, thick tapering dendrites arise from the soma and they have spines with long thin stalks and complex end bulbs that may appear mushroom shaped. Large axon terminals with round synaptic vesicles contact both somal and dendritic spines of mossy cells. These terminals are identical to mossy fiber tufts and when they contact an impregnated dendrite they fail to contact adjacent neuronal profiles. The axon initial segment of mossy cells arises from an axon hillock and is contacted by a few terminals that form symmetric synapses. The axon terminals of mossy cells are small and form asymmetric synapses. The results from HRP retrograde studies indicate that mossy cells are labeled following HRP injections into the contralateral dentate gyrus. These results indicate that the mossy cells: 1) are contacted by numerous mossy fibers that arise from granule cells and 2) have commissural projections that probably excite the granule cells in the contralateral dentate gyrus. Therefore, the mossy cell is an important hilar neuron that is dominated by synaptic input from granule cells. (Supported by N.I.H. grant NS-20228).

PHOSPHORYLATION IN THE CENTRAL NERVOUS SYSTEM OF LONG-TERM SENSITIZED Aplysia. Saitoh, T. Howard Hughes Medical Institute and the Center for Neurobiol. & Behavior, Columbia Univ. Col. P & S, New York, NY 10032.

Sensitization of the gill and siphon-withdrawal reflex in Aplysia, a simple form of learning, has been studied extensively by Kandel and his colleagues and has been shown to involve an enhancement of transmitter release from the sensory neurons on their central target cells (Kandel et al., 1976, C.S.H.S.Q.B. 40: 465). Considerable evidence indicates that this synaptic modulation underlying short-term sensitization is mediated and maintained by cAMP with the resultant activation of protein kinase. However, the maintenance of long-term sensitization does not seem to involve cAMP elevation (Bernier et al., 1982 J. Neurosci. 2: 1682).

It has been suggested (DeLorenzo et al., 1979 P.N.A.S. 76: 1838) that kinase B (the Ca^{2+}/calmodulin-dependent kinase) plays a role in transmitter release. If so, enhanced activity of kinase B may underlie the long-term sensitized state. We prepared sensitized animals, using 4 trains of 4 electric shocks (50 mA, 60 Hz) for 4 days to the tail (Castellucci, Frost, Hawkins, and Kandel, in preparation). One day later, the abdominal ganglia were dissected out from sensitized animals and from non-treated animals, and neuronal components were homogenized and assayed for Ca^{2+}/calmodulin-dependent kinase activity.

In sensitized animals, this kinase activity was higher than control by 39%. At the same time, the degree of phosphorylation of a M_r 130,000 protein was higher than control by 96%. The total phosphorylation of the sensitized sample was higher than control by 31%, indicating that the change in phosphorylation of this M_r 130,000 protein was higher than the background change. In the presence of EGTA, the phosphorylation of this protein was reduced by only 24%. We have found previously that once autophosphorylated, the kinase B does not need Ca^{2+}/calmodulin for activity. Therefore, we do not know if the phosphorylation of the M_r 130,000 protein in long-term sensitized animals is due to this persistently activated Ca^{2+}/calmodulin-dependent kinase or to an unidentified kinase. We are currently testing the hypothesis that the phosphorylation of M_r 130,000 protein is involved in the long-term sensitized state.

MORPHOLOGICAL CORRELATES OF PASSIVE AVOIDANCE TRAINING IN THE CHICK FOREBRAIN. M.G. Stewart, Brain Research Group, Department of Biology, The Open University, Milton Keynes, MK7 6AA, England.

The paradigm of one-trial passive avoidance training (PAL) in which one-day old chicks are trained to avoid pecking a bead coated with the aversive tasting substance, methyl anthranilate (MeA), has been used for a number of years in our laboratory as a model for the cellular correlates of memory formation. Autoradiographic studies employing the ^{14}C-2-deoxyglucose technique have indicated an elevation in incorporation of glucose, or its phosphorylated product, in 3 regions of the forebrain of MeA-trained birds compared with those of water trained controls (W-control) - the medial hyperstrium ventrale (MHV), paleostriatum augmentatum (PA) and lobus parolfactorius (LPO) (Kossut, M. and Rose, S.P.R. Neurosci. (in press)).

A quantitative stereological investigation was made of synapses in left and right hemispheres in each of these three regions in MeA-trained and W-control chicks. There are no significant differences in the numerical density of synapses ($N_{v.syn}$) in any of the regions, either between hemispheres or between MeA-trained and W-control chicks. However, a hemispheric asymmetry exists in the length of the post-synaptic thickening ($\bar{D}$) in the MHV and LPO of W-control chicks (R > L by approximately 10%), and these differences disappear on MeA-training. There are no significant differences in $\bar{D}$ in the PA either between hemispheres, or between MeA-trained or W-control chicks.

Measurements of additional synaptic parameters (numerical density of synaptic vesicles ($N_{v.ves}$) and the volume density of the pre-synaptic bouton ($V_{v.syn}$) were made in each hemisphere of the MHV of MeA-trained and W-control chicks. No differences were found in $V_{v.syn}$ between either hemisphere of W-control chicks but following MeA-training $V_{v.syn}$ was 23% greater in the left than in the right hemisphere. $N_{v.ves}$ was 12% greater in the left than in the right hemisphere of W-control chicks, but following MeA-training these differences are reversed. These data are discussed in terms of recent evidence that there is lateralization of brain function in chicks (Rogers, L.J., Nature, 297, 223-225, 1982).

HIPPOCAMPAL NEURONS SHOW CONSISTENT PLACE FIELD ACTIVITY FOR EXTENDED PERIODS OF TIME IN A STABLE ENVIRONMENT
P. J. Best and L. T. Thompson, Department of Psychology, University of Virginia, Charlottesville, Virginia 22901.

The hippocampus is one area of the brain that shows a high degree of plasticity. Evidence comes from the study of a variety of phenomena--sprouting, kindling, long-term potentiation, and changes in neuronal activity during behavioral conditioning.

We report here evidence for extraordinary stability of hippocampal cellular activity over very long periods of time. This experiment follows a recent study which found that the same hippocampal neurons show place field activity and show conditional responses, and that behavioral conditioning does not modify existing field activity (P.J. Best and L.T. Thompson, Neurosci. Abstracts, 1984).

Rats were implanted with a bundle of ten 32u electrodes.. The electrode bundle was advanced until well isolated hippocampal unit activity with 4:1 signal to noise ratio was found on one or more electrodes. The animals were placed on a six-arm radial area maze until they made at least eight visits to each arm. Place fields were determined by automatic registration of the rat's location along with on-line computer analysis of unit activity. On subsequent days the unit signals were examined and if the activity from the same cell appeared to be present on the same electrode, the animal was run again on the maze and place field activity was redetermined. This procedure was repeated at irregular intervals until the location of the field changed or the cell was lost. Then, the electrodes would be moved until another cell was encountered. Also, the animal periodically underwent behavioral conditioning in a different environment and conditioned cellular activity was analyzed.

Occasionally, a cell would disappear and another cell would appear on that channel. That cell always had a different field, as did all new cells encountered by moving the electrode. In every case in which we were certain on physiological evidences that we were recording from the same cell from day to day, the place field did not change.

In no case did we find evidence that the place field of a cell changed over time. Such a conclusion would be hard to differentiate from the shift of the recording electrode from one cell to a neighbor.

However, if the field does not change it is unlikely that the recording electrode moved to a neighboring cell, unless all neighbors have the same field.

To date, we have found stability of place field activity for up to 156 days!

NORMAL LATENCY VARIABILITY IN THE AUDITORY EVENT-RELATED POTENTIAL. H.J. Michalewski*, D. Prasher* and A. Starr. Department of Neurology, University of California, Irvine, CA 92717.

Traditional averaging procedures may sometimes obscure features of the event-related potential (ERP), such as component variability. We have attempted to estimate the latencies of N1, P2, N2, and P3 in the ERP waveform on a trial-by-trial basis. In addition to measures of component variability, the relationship among components to the prediction of P3 latency was examined.

Auditory ERPs were collected from a group of normal (N = 12) individuals in an oddball paradigm. Subjects were required to detect an occasional high frequency tone (640 Hz) interspersed among a sequence of low frequency (440 Hz) tones. Scalp potentials were recorded from midline sites Fz, Cz, and Pz referenced to linked earlobes. Each tone trial was digitized and saved to disk. Averages were computed to target (high) tones (N = 60). The single trial analysis used a modified version of the Woody correlational-template technique to identify the major peaks of the ERP. Separate templates, derived from the individual peaks of the average waveform, were used to define component shapes. Estimates of peak latency were computed separately for each component successively.

Based on the results of the Woody analysis, the following mean peak latencies (msec) and (standard deviations) were found: (1) for Pz, N1 = 91.1 (20.2), P2 = 170.2 (27.1), N2 = 242.5 (51.9), and P3 = 324.3 (52.1); (2) for Cz, N1 = 88.9 (16.4), P2 = 166.8 (24.1), N2 = 246.9 (55.5), and P3 = 341.1 (59.9); and (3) for Fz, N1 = 89.9 (16.8), P2 = 172.1 (26.0), N2 = 244.4 (53.9), and P3 = 327.3 (58.9). Analysis of peak variances indicated that the variance of N1 was significantly less than the variance of P2, the variance of P2 was less than either the variance of N2 or P3, but that the variance of N2 was not different from the variance of P3.

The contribution of various peaks to the prediction of P3 latency was evaluated in a series of regression analyses. Predictors of P3 included N1, P2, and N2 considered separately or in combination. Over 60% of the variance of P3 was accounted for by N2. Including N1 and/or P2 did not add to the prediction of P3. Measures of variance and the relationships among peaks may add useful information in characterizing the ERP components.

Supported in part by Grant #NS11876.

GENERATOR OF P300 IN THE CAT. T. O'Connor and A. Starr. Department of Neurology, California College of Medicine, University of California, Irvine, CA 92717.

Intracranial recordings of long-latency evoked potentials were obtained from an animal model of the P300. Muscle-relaxed, artificially-respired cats were presented with a variant of the "oddball" paradigm in which a "rare" 4KHz stimulus was intermixed with a "frequent" 1KHz stimulus. A pupillary dilation served as a behavioral index to the rare tone. A fixed skull electrode near the vertex served as a control recording site while electrodes were advanced into the brain through chronically implanted cannulas.

At intracranial locations waveforms associated with the rare tone generally differed substantially from the frequent stimulus waveforms in that the former usually manifested components of greater amplitude. The P300, which is positive at the vertex and dura, appeared as a negative component 4-6 mm below the surface of the marginal gyrus. Increasing the probability of the rare stimulus decreased the amplitudes of both the intracranial negative component and control P300. In the hippocampus a component occurred with a latency about that of the P300 which phase reversed between the dorsal and ventral aspects of that structure. Ablation of several mm of the marginal gyrus bilaterally modified significantly the P300 recorded from the vertex without affecting pupillary dilation. These results suggest that the cat P300 originates, at least in part, from the cortex of the marginal gyrus.

Supported by NIH Grant #NS11876-08

MONKEYS WITH LESIONS OF HIPPOCAMPUS AND AMYGDALA EXHIBIT EVENT-RELATED BRAIN POTENTIALS THAT RESEMBLE THE HUMAN P300 WAVE. K.A. Paller, S. Zola-Morgan, L.R. Squire, and S.A. Hillyard. Depts. of Neurosciences and Psychiatry, U.C.S.D. Sch. of Med., and VA Medical Center, La Jolla, CA 92093.

Perceptual and cognitive events in humans are reliably correlated with neurophysiological measures known as event-related brain potentials (ERPs). Among these, the P300 wave has been considered to reflect information processing related to expectancy, orienting, and memory. Medial temporal lobe brain structures have been implicated as possible sources of this electrical activity. To improve our understanding of the neural bases of these potentials and the associated cognitive processes, similar potentials have been investigated in the monkey.

Eight Cynomolgous monkeys (Macaca fasicularis) had screw electrodes chronically implanted at selected skull sites. "Oddball" sequences of randomly ordered 1450 Hz (90%) and 300 Hz (10%) tone bursts having no conditioned significance were presented with a one sec interstimulus interval. ERPs to the rare tones included a prominent positive wave between 150 and 450 msec after stimulus-onset, of maximal amplitude at central midline sites. Similar ERPs were elicited by stimuli that resembled monkey vocalizations. During other sequences in which two stimuli were equally probable, the amplitude of the late positive wave varied systematically in the manner of the human P300 component; the positivity was largest when the evoking stimulus differed from previous stimuli. Four monkeys were trained in a tone-frequency discrimination task. A similar late positive ERP was elicited by the task-relevant rare tones under these conditions, and its amplitude gradually habituated when manipulandum and reward apparatus were removed.

Similar ERPs were recorded from humans under comparable conditions. Cross-species parallels suggest that the monkey late positive waves and the human P300 waves may reflect homologous neurophysiological processes.

Each of five monkeys with bilateral medial temporal lobe resections exhibited late positive ERPs, although waveforms were altered in some conditions. ERP differences were analyzed in between-group comparisons (three intact monkeys and three lesioned monkeys) and within-group comparisons (two monkeys pre- and post-surgery). These data indicate that at least some late positive activity in the monkey is not dependent on the hippocampus or amygdala, thus supporting the hypothesis that these brain structures are not the exclusive generators of the P300 in humans.

EVENT-RELATED POTENTIALS IN SQUIRREL MONKEYS EXHIBIT SIMILARITIES TO HUMAN SLOW POTENTIALS. J. Pineda ***, S. Foote* ***, H. Neville**. Department of Neuroscience, UCSD, *Department of Psychiatr UCSD, **Salk Institute, and ***Research Institute of the Scripps Clinic, La Jolla, CA.

Event-related potentials (ERPs) were recorded from the brain surface of squirrel monkeys in paradigms similar to those in which specific ERPs have been studied in humans. Auditory stimuli were presented to passive monkeys and to those trained to make specific responses. Seven squirrel monkeys (Saimiri sciureus) were chronically implanted with skull-screw electrodes at midline (Fz, Cz, Pz) and lateral (F3, F4, T3, T4, P3, P4) sites.

Active paradigm. Monkeys were trained to obtain a reward by making a delayed bar-press response to tones presented on average once every six seconds. A light signalled "time-in", during which responses to the tone were rewarded, and "time-out", when similar tones were presented but no reward occurred. ERPs to the tones included: a prominent positivity around 30 msec (P30), followed by an N80-P140 complex. Furthermore, "time-in" stimuli followed by a correct response elicited a prominent negative potential that began around 200 msec, peaked at 400 msec, and was of approximately 400-500 msec duration. This waveform was largest over frontal brain regions along the midline, and larger over the right than the left hemisphere. A similar waveform has been reported in humans in response to repetitive stimuli separated by interstimulus intervals of several seconds.

Passive paradigm. Stimulus sequences composed of 2 and 6 kHz tones were presented in pseudo-random order at one-second ISIs. The probability of occurrence for the tones varied from low (10%), to intermediate (50%) to high (90%). ERPs to the tones displayed early (< 200 msec) components similar to those seen in the active paradigm. Additionally, infrequent tones elicited a sustained positive potential that began about 300 msec and peaked around 400-500 msec. The amplitude of this potential, which was largest at frontal and right lateral sites, was found to be inversely related to stimulus probability. This component appears similar to the human P3a observed in analogous paradigms, although specific differences were also evident.

In summary, we have recorded ERPs in monkeys which appear to be analogous to those previously observed in humans. This provides an opportunity to explore the neural substrates of electrical events which have been correlated with psychological processes. We are beginning studies that will explore the hypothesis that brain monoamines, i.e., norepinephrine, dopamine, and/or serotonin, may produce or modulate these events.

Supported by USPHS grants NS 21379 and NS 21384 (S.F).

EVENT RELATED POTENTIALS TO SIMULTANOUS AUDITORY AND VISUAL STIMULI. C. E. Rosenberg, L. Meyer, A. Starr
Electrodiagnostic Laboratory, Univ. of California at Irvine Med. Center, Orange, CA 92668.

Event related potentials were recorded from 11 normal subjects ages 20 to 36. In three different reaction time tasks: an auditory tone discrimination. A visual discrimination between an "X" vs "O", and a bimodal task presenting the stimuli from the first two tasks simultaneously. The bimodal and visual tasks were 295, 363 and 363 msec. The sum of the visual and auditory target averages was compared to the bimodal target average. The P3 amplitude of the sum was over twice that of the bimodal P3. Five of the subjects were tested with bimodal stimuli with the auditory stimulus occuring 50 to 200 msec after the visual stimulus. The four combinations of tone and character produced four different averages from each test with a different auditory onset time. All the averages of each test were correlated with each other over their first 500 msec. The correlation between averages with the same auditory stimulus was large with the similtaneous stimuli but as the auditory stimulus was delayed this correlation decreased and the correlation between averages sharing the same visual stimulus increased. These results illustrate modualtion of the electrophysiologic response to one sensory modality by another sensory modality.

CAN SEPTAL TRANSPLANTS RESTORE SINGLE UNIT ACTIVITY IN THE HIPPOCAMPUS? M.L. Shapiro, D. Simon*, & D.S. Olton, Dept. of Psychology, Johns Hopkins University, Baltimore, MD, 21218, F.H. Gage, A. Bjorklund*, & U. Stenevi*, Dept. of Histology, Universtiy of Lund, Lund, Sweden.

Transplants of embryonic septal tissue can restore maze performance in rats given fimbria-fornix (Ffx) lesions. However, transplants can produce greater impairments in the performance of maze tasks than lesions alone (Gage, Bjorklund, and Stenevi, in press). The patterns of transplant innervation of the hippocampus have not yet been distinguished histologically in these two cases. The present study investigated the effects of transplants of embryonic septal tissue upon single unit activity in the hippocampus of four groups of rats: normal rats, those given Ffx lesions, those given Ffx lesions and transplants that improved performance on spatial memory tests (imp/smart), and those given Ffx lesions and transplants that impaired maze performance (imp/impaired).

Theta unit activity was recorded from the CA-1 layer of the dorsal hippocampus during two behaviors: (1) an appetitive behavior in which rats walked on an elevated track during recording, (2) a consummatory behavior in which rats drank chocolate milk from a drinking tube.

In normal rats, high frequency theta unit activity was organized into 7 hz spike trains during appetitive behavior, while low frequency activity was not organized into rhythmic spike trains during consummatory behavior. In rats given Ffx lesions, the activity of theta units was not organized into rhythmic spike trains, while overall firing rate still increased during appetitive behaviors relative to consummatory behavior. In imp/smart rats, the activity of theta units appeared to be organized into rhythmic spike trains, and overall firing rate increased during appetitive behavior relative to consummatory behavior. In imp/impaired rats, the activity of theta units was not organized during appetitive behavior, and little difference in firing rate distinguished the two behaviors.

These results suggest that (1) transplants alter the activity of hippocampal neurons, (2) the type of alteration may be critical to recovery of function brought about by transplants, and (3) restoration of behavior may occur to the extent that patterns of modulation resemble those found in normal rats. (Supported by NIMH P316123.)

PLASTICITY OF FREQUENCY TUNING OF SINGLE NEURONS IN AUDITORY CORTEX DURING LEARNING. N.M. Weinberger, D.M. Diamond and T. McKenna. Center for the Neurobiology of Learning and Memory and Dept. of Psychobiology, University of California, Irvine, Irvine, CA 92717

Numerous studies of classical and instrumental conditioning have demonstrated that the evoked responses of neurons in sensory cortex change during learning. Consistent with earlier multiple unit studies, we previously recorded from single neurons in auditory cortex and found that most developed discharge plasticity during learning (Behav. Neurosci., 98:171-188; 189-210, 1984). In this report, we address the issue of the functional significance of the evoked plasticity which develops as the meaning of sounds changes during learning. Our working hypothesis is that discharge plasticity to an acoustic signal represents changes in the sensory response properties of auditory cortical neurons. This "retuning" is viewed as a dynamic process in which the discharges of cortical neurons convey aspects of the meaning as well as of the physical parameters of sounds.

Single unit activity was recorded in chronically prepared cats under neuromuscular blockade to ensure stimulus constancy. The training stimuli were a tone (CS) and electrodermal stimulation (US); pupillary dilation to the CS served as the indicator of learning. Frequency tuning was determined by presenting isointensity tones for a range of frequencies before and after a sensitization phase (CS/US unpaired) to control for non-associative effects, and following conditioning (CS/US paired) and extinction (CS alone).

Evoked activity to the CS frequency was changed as a function of CS/US pairing, as reported previously. Of particular importance, frequency tuning was also altered by conditioning. This effect was associative because frequency tuning was not changed by sensitization procedures. Further, alterations in tuning induced by conditioning were reversed by extinction.

These data indicate that aspects of the receptive field properties of auditory cortical neurons, such as frequency tuning, can be modified by learning.

Supported by a grant from the Monsanto Co.

BRAIN BETA-ADRENERGIC MECHANISMS WOULD PARTICIPATE IN NALOXONE-INDUCED ENHANCEMENT OF MEMORY IN MICE. C.M.Baratti and I.B.Introini. Cátedra de Farmacología. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires. RA-1113 Buenos Aires. ARGENTINA.

The opioid receptor antagonist naloxone (0.1 mg/kg, ip) facilitates retention of a step-through one-trial inhibitory avoidance response when administered to male Swiss mice immediately after training, as indicated by performance on a retention test 48 hr later. The facilitatory action of naloxone was antagonized by the selective brain noradrenaline depletion induced by the neurotoxin DSP 4 (50 mg/kg, ip, 7 days before training). Pretreatment with the noradrenaline uptake inhibitor desmetylimipramine (10 mg/kg, ip, 30 min) but not with the serotonin uptake inhibitor fluoxetine (5 mg/kg, ip, 30 min), prevented this antagonism. These results suggest the participation of brain noradrenergic mechanisms in naloxone-induced memory facilitation and rule out the possibility that the antagonism observed may be due to an unspecific action of DSP 4 on another neuronal system. The simultaneous administration of the central beta-adrenoceptor blocker l-propranolol (2 mg/kg,ip) but not its stereoisomer d-propranolol (2 mg/kg,ip), the peripheral beta-adrenoceptor blocker sotalol (2 mg/kg, ip), the central alpha-adrenoceptor blocker phenoxybenzamine (10 mg/kg, ip) or the peripheral alpha-adrenoceptor blocker phentolamine (10 mg/kg, ip), prevented the effects of naloxone on memory. These findings would indicate that central beta-adrenergic but neither central nor peripheral alpha-adrenergic mechanisms participate in the behavioral effects induced by naloxone in mice. Naloxone (0.1 mg/kg, ip) potentiated the effects of the central beta-adrenoceptor agonist clenbuterol (0.001-1.000 mg/kg, ip), which facilitates or impairs retention as a function of the dose injected. This potentiation suggests that the facilitatory action of naloxone on memory would be the result of the release of central beta-adrenergic mechanisms from an inhibition induced by opioid peptides probably released during or immediately after training (Izquierdo,I., TIPS, 3:455, 1982). Taking into account that DSP 4 exerts its selective neurotoxic action upon noradrenergic nerve terminals in several brain regions innervated by the locus coeruleus, the interaction between DSP 4 and naloxone suggests that the locus coeruleus noradrenergic system is required for naloxone-induced memory facilitation. This adrenergic influence should be mediated by beta-adrenoceptors.

EFFECTS OF THE CENTRAL BETA-ADRENOCEPTOR AGONIST CLENBUTEROL ON MEMORY CONSOLIDATION IN MICE. I.B.Introini and C. M.Baratti. Cátedra de Farmacología. Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires. RA-1113 Buenos Aires. ARGENTINA.

Posttraining injections of the central beta-adrenoceptor agonist clenbuterol (0.001-1.000 mg/kg, ip) to male Swiss mice significantly affected retention of an inhibitory avoidance response in a non-monotonic fashion as a function of the dosage of clenbuterol, as indicated by performance on a retention test 48 hr later. The dose-response curve adopted an inverted-U form. The doses of 0.010 and 0.030 mg/kg significantly facilitated retention while the doses of 0.300 and 1.000 mg/kg significantly impaired it. Both enhancement and impairment of retention were time-dependent since the effects on retention decreased as the training-treatment interval was increased. The facilitatory effects of clenbuterol on retention were not due to a punitive action of the drug since the posttraining administration of clenbuterol to unshocked mice did not lengthen their latencies to step-through during the retention test. The simultaneous administration of the central beta-adrenoceptor blocker l-propranolol (2 mg/kg, ip) but neither its stereoisomer d-propranolol (2 mg/kg, ip) nor sotalol (2 mg/kg, ip), a peripheral beta-adrenoceptor blocker, prevented both effects of clenbuterol on retention. These findings suggest that central beta adrenergic mechanisms may modulate memory consolidation Pretreatment with the selective noradrenergic neurotoxin DSP 4 (50 mg/kg, ip, 7 days before training) but not with the aziridinium form of the drug which crosses the blood-brain barrier poorly, shifted the dose-response curve of clenbuterol to the left. DSP 4 selectively depletes noradrenaline from neurons mainly originating from the locus coeruleus and as a consequence of this increases beta-adrenoceptors density in some regions of the brain (Dooley et al., Neurosci. 9:889, 1983). Thus the clenbuterol dose-response curve shift observed may be due to the development of supersensitivity to beta-adrenoceptor agonists. Taken together these results suggest that the effects of clenbuterol on memory are induced in brain regions which are at least in part innervated by the locus coeruleus noradrenergic system.

AMPHETAMINE DISRUPTS BOTH WORKING AND REFERENCE MEMORIES OF RATS TRAINED IN A RADIAL MAZE. W.W. Beatty, R.A. Bierley and J.G. Boyd. Dept. of Psychology, North Dakota State Univ., Fargo, ND 58105.

Provided that a delay is imposed between the to-be-remembered event (TBRE) and the retention test moderate doses of amphetamine impair retention in a number of working memory (WM) paradigms. Explanations for these effects vary; it has been suggested that amphetamine speeds the loss of information from storage, increases the impact of interfering stimuli present during the retention interval or simply causes nonspecific performance changes.

To test these competing views rats were trained in a 12-arm radial maze with 6 baited and 6 unbaited arms. This permitted an assessment of amphetamine effects on WM as well as reference memory (RM). Since much other data indicate that amphetamine does not impair and often improves long-term memory (LTM, of which RM is a component), observing that amphetamine increased both WM and RM errors equivalently would support a performance as opposed to a memorial view of the effects of amphetamine on WM and perhaps STM in general.

After stable performance was achieved the rats were treated with 0.5, 1 or 2 mg/kg amphetamine sulfate 10 min before testing. When no delay was imposed during the run none of the drug doses affected performance. When a 5 min delay was imposed after 3 successful choices the 2 mg/kg dose increased both WM and RM errors to a comparable extent. Lower doses were ineffective.

Previous findings that amphetamine does not impair and often enhances LTM as well the inability of the drug to disrupt WM when it is given immediately after the TBRE suggest that amphetamine does not degrade memory storage. While it is possible that amphetamine disrupts spatial memory by increasing the impact of interfering stimuli, this idea is not attractive because the rat's spatial WM is highly resistant to retroactive interference. The most likely explanation for the finding that amphetamine disrupts both WM and RM only if a brief delay is imposed between the TBRE and the retention test is that in a state of heightened arousal (caused by the drug) the rat is unable to maintain attention to the cues that normally guide accurate performance because the operations associated with imposing the delay disrupt its attention to these cues.

EPINEPHRINE FACILITATES INHIBITORY AVOIDANCE RETENTION OF ADRENAL DENERVATED RATS TREATED WITH A HIGH DOSE OF DSP4.

C. Bennett*, S. Kaleta*, M. Arnold*, and J.L. McGaugh.
Center for the Neurobiology of Learning and Memory, University of California, Irvine, CA 92717

Brain norepinephrine (NE) levels within 30 minutes after training have been correlated with retention performance (Beh. Biol. 24, 168). This result suggests that the release of brain NE modulates memory formation. Further, epiniphrine (EPI) given peripherally in doses that affect retention, can potentiate the decrease in CNS NE after training (Beh. Biol. 23, 509). Therefore systemic EPI may influence memory formation by triggering the release of central NE. In the present experiment we tested the possibility that the memory modulatory effects of peripherally administered EPI, is blocked by central NE depletion.

Male Sprague-Dawley rats were adrenal denervated to deplete adrenal catecholamines (Br. Res. 201, 236). Two weeks after the adrenal surgery, they were given 0.9% saline (Control) or N-(2-chloroethyl) N-ethyl 2-bromobenzylamine (DSP4) (100 mg/kg, ip) in a divided dose to deplete central and peripheral NE (Br. J. Pharm. 58, 521). The DSP4 was synthesized by two of us (Arnold & Bennett) after the method of Krueger & Cook (Arch. Int. Pharm. 218, 96). Two days after the second dose, while sympathetic as well as central NE stores were depleted, the rats were trained on a one-trial step-through inhibitory avoidance task (8). Any animal which did not step through within 90 seconds was eliminated. Immediately after training, each rat received saline (Sal) or EPI (0.1 mg/kg, sc). Retention, measured as the latency to step through, was tested 24 hours later.

Significantly more DSP4 (8/31) than Control (1/28) rats were eliminated for failing to step through within 90 seconds (Chi Sq. = 4.04, $p < 0.05$), however, the entrance latencies of the DSP4 and Control rats which were trained did not differ significantly. The retention scores of the DSP4/Sal and the Control/Sal groups did not differ significantly, therefore, DSP4 does not appear to affect acquisition or retention of this task. However, the difference in the entrance latencies suggests that DSP4 treatment may impair spontaneous activity or response initiation. EPI significantly enhanced the retention of both Control and DSP4 groups. These data suggest that the memory modulatory effects of systemic EPI are not likely to be explained by an EPI-stimulated release of central NE.

Supported by USPHS Grants MH12526 & AG00538 (to JLMcG).

MET-ENKEPHALIN: DIFFERENTIAL EFFECTS IN THE HIPPOCAMPUS.

L. Cahill*, H. Haigler, and R. Kochman (SPON: J. Bloss).
Searle Research & Devlopment, 4901 Searle Parkway, Skokie, IL 60077.

Met-Enkephalin (ME) has been reported to produce an excitatory effect on neuronal firing when administered microiontophoretically in the hippocampus, but there was no reported histological confirmation of the recording sites (Zigelgansberger, W. et al. Science 205:415, 1979). We report here that the response to ME depends on the area of the hippocampus from which the recording was obtained.

The experiments were carried out as follows: Fisher 344 rats (350-400 gms) were anesthetized with chloral hydrate (CH) (400 mpk) administered i.p.; anesthesia was maintained by supplemental doses of CH. Microiontophoretic experiments were carried out using the techniques described previously (Hosford, D. and Haigler, H., J. Pharmacol. Exp. Therap. 213:355, 1980). When presumed hippocampal neuronal activity was encountered (i.e., negative action potentials that usually occurred in bursts of decreasing amplitude) the response to varying ejection currents of both ACh and ME were obtained. Drugs were ejected by a positive direct current (10-100 nA) applied to the drug barrel for a period of 50 seconds. At the end of an experiment fast green (FG) was ejected electrophoretically from the recording barrel, which was filled with 2M saline saturated with FG. The FG mark served as a reference point to localize the recording sites. The results are summarized below:

Location in Hippocampus	N	Increase N (%)	Decrease N (%)	No Effect N (%)
CA1	32	5 (16)	3 (9)	24 (75)
CA2,3,4	20	18 (90)	0	2 (10)

Note: Responsive and non-responsive neurons were found using the same micropipette

ACh increased firing of all of the above neurons indicating that the differential effect of ME on firing rates was not artefactual. These data may account for the variation in reports of percentage of hippocampal pyramidal cell excited by ME. These data also indicate that ME does not have a uniform effect on neurons in the hippocampus. The functional significance of this observation remains to be determined.

D-6

AMINO ACID AND GLUCOSE ENHANCEMENT OF MEMORY STORAGE: POSSIBLE MEDIATORS OF EPINEPHRINE EFFECTS ON MEMORY. P.E. Gold. Department of Psychology, University of Virginia, Charlottesville, VA 22901.

When administered shortly after training, peripheral epinephrine (E) injections facilitate memory of learned responses for both appetitive and aversive experiences. However, peripheral E apparently does not enter the brain in large amounts and the mechanisms by which plasma E might act on memory are as yet unclear. One of the classic actions of E is to mobilize metabolic stores in response to stress. The present experiments examined the effects of posttraining injections (s.c.) of both amino acids (AA; a solution containing 24 amino acids) and glucose (Glu) on retention of inhibitory avoidance training in male Sprague-Dawley rats.

The results indicate that both Glu and AA are very effective in enhancing later retention performance. Animals which received the AA solution of Glu had retention latencies significantly higher than those of saline controls. Injections delayed by 1 hr after training had no significant effect on later retention performance.

Adrenergic antagonists attenuate the effects on memory of E and most other memory modulators. If E acts on memory by increasing plasma levels of such substances as AAs and Glu, the effects of these drugs on memory should not be influenced by pretreatment with adrenergic antagonists. Indeed, antagonists administered prior to training and treatment did not attenuate the effects of AAs on memory. Preliminary evidence suggests that Glu effects on memory were also not reduced in animals which received propranolol.

The findings of these studies suggest that E may act on memory by increasing the availability of AAs and Glu for use in metabolism in the central nervous system as well as peripherally. If so, the results suggest that epinephrine effects on memory utilize many of the classic actions of the hormone on organismic physiological responses to stressors. Such metabolic effects would provide an intermediate step between plasma E and its large effects on many brain functions including memory storage.

Supported by NIMH grant MH 31141 and by a fellowship from the James McKeen Cattell Foundation.

D-7

Lysine-vasopressin (LVP) Enhances Retention of a Spatial Discrimination in Rats. M. P. Hammer. Dept. of Psychology, University of Alberta, Edmonton, Alberta, T6G 2E1.

The neuropeptide hormone vasopressin has been claimed to facilitate long-term retention of memory in animals. Published studies supporting this view have relied almost exclusively on the use of aversively motivated tasks. Studies employing appetitive tasks to assess retention enhancement effects of VP have yielded either negative or ambiguous outcomes. In light of this and other evidence, several authors have suggested that VP may be primarily involved in potentiating the learning or performance, but not retention, of aversive tasks.

This study demonstrates a limited enhancing effect of post-training treatment with lysine-vasopressin (LVP; 6ug/kg) on rats' retention of a food-motivated spatial discrimination. Rats were given massed training on a left/right T-maze discrimination, injected with LVP and tested for retardation of discrimination reversal 48 hours later. LVP-treated subjects trained to a criterion of 8/10 correct on the original discrimination took significantly more trials to reach the reversal criterion than saline controls (24.6 vs. 18.9; $p=.037$). LVP and saline controls given an additional 20 overtraining trials did not differ. The study suggests that vasopressin can facilitate long-term retention of nonaversive information and that procedural rather than motivational differences may account for the discrepant findings of published aversive and appetitive studies.

(Supported by an AMHAC grant to M. Hammer, and NSERC grants to Dr. D. S. Grant and Dr. R. Walley)

D-8

FUNCTIONAL ACTIVITY IN THE BRAIN OF SOCIALLY DEPRIVED RATS PRODUCED BY AN ACTIVE AVOIDANCE TEST AFTER HOE 175 AND CLOBAZAM TREATMENTS: A 2-DEOXYGLUCOSE STUDY. F.J. Hock[1,2] and H. Scheich[2].
(1) HOECHST AG, P.O. Box 800320, D-6230 Frankfurt/M. 80, FRG; (2) Technical University Darmstadt, Institute for Zoology, D-6100 Darmstadt, FRG.

The 2-deoxyglucose (2-DG) autoradiographic method was used to map the activity in the brain of socially deprived rats during an active avoidance test. The effects of Hoe 175 and clobazam during this learning test were investigated with this method. Animals were socially deprivated for 5 weeks. On the first day the animals were trained (50 trials) to avoid a footshock by jumping on a platform. Each trial consisted of a 10 sec light signal followed by 20 sec footshock (400 µA) after which there was a 50 sec intertrial interval. The retention test trial was run 24 hrs later with the same parameters. During training and testing the total of avoidance responses was scored. Hoe 175 and clobazam were administered orally 60 min before second day testing. 2-DG, 18 µCi/100 g body weight , was administered intraperitoneally 50 min after the test substance. Hoe 175 increased the avoidance score by 14 % and clobazam by 11 % as compared to controls. Autoradiographs were analyzed with a two dimensional densitometric method (Gonzales-Lima and Scheich, Brain Res. 299, 201 - 214 (1984). The analysis of limbic brain structures, so far, showed a 24 % reduction of optical density in the habenular nucleus in Hoe 175 treated rats and a smaller decrease under clobazam.

D-9

EFFECTS OF PERIPHERAL EPINEPHRINE, 4-OH AMPHETAMINE, AND D-AMPHETAMINE ON THE MAINTAINED DISCHARGE OF CELLS IN THE LOCUS COERULEUS. R. N. Holdefer and R. A. Jensen. Developmental Biopsychology Laboratory, Southern Illinois University, Carbondale, IL 62901.

Post-training peripheral injections of d-amphetamine, 4-OH amphetamine, and epinephrine enhance memory storage processes. One possible mechanism for their common effects is that these treatments may facilitate central noradrenergic (NE) transmission. Therefore, the goal of the present study was to determine whether peripheral administration of d-amphetamine, 4-OH amphetamine, and epinephrine produce similar effects on the maintained discharge of cells in a major NE nucleus, the locus coeruleus (LC), in parallel with their common facilitatory effects on memory.

The maintained discharge of single cells in the LC was monitored in halothane-anesthetized rats after intraperitoneal administration of d-amphetamine (1.0 mg/kg), 4-OH amphetamine (0.82 mg/kg), epinephrine (50.0 µg/kg), or control injections of saline vehicle. These doses and this route of administration have been shown to enhance memory storage processes in behaving animals (Izquierdo, I. & Dias, R.D., Psychoneuroendocrinology, 8:81, 1983; Martinez, Jr., J.L., et al., Brain Res., 195:433, 1980).

Cells initially identified on the basis of waveform, rate of maintained discharge (1.41 Hz, S.E.M. = 0.15) and excitation and subsequent inhibition by paw-pinch, and later shown histologically to have been in the LC, were studied. The maintained discharge of these cells from 5 min to 90 min after drug administration was profoundly depressed by d-amphetamine as compared to the activity of cells during the same time period after saline control injections (F (1,19) = 52.2, $p < .01$). Maintained discharge following amphetamine was decreased to 13.3% of that seen after saline administration. However, no differences in maintained discharge during this time period was noted after either 4-OH amphetamine (F (1,22) = 0.66, p = n.s.) or epinephrine (F (1,26) = 0.58, p = n.s.) as compared to control animals .

Despite the common capacity of d-amphetamine, 4-OH amphetamine, and epinephrine to enhance memory when given after training at the doses used in this study, these treatments differ markedly in their effects on the firing rate of LC cells. Taken together these findings demonstrating differences in the central effects of 4-OH amphetamine, d-amphetamine, and epinephrine in the anesthesized rat do not support the hypothesis that these different treatments enhance memory storage processes through some common action on the LC.
(Supported by a research grant from the Office of Research Development and Administration, SIU-C.)

D-10

B-ENDORPHIN EFFECTS ON RETRIEVAL, AND THE NEURAL PATHWAYS INVOLVED IN THE BRAIN B-ENDORPHIN RELEASE CAUSED BY TRAINING. I. Izquierdo and C.A. Netto. Depto. Bioquím, UFRGS, 90000 Porto Alegre, Brazil.

B-endorphin given before or after training inhibits retrieval of many tasks 24 or more hr later, an effect that is reversed by a new injection of the substance prior to testing (Izquierdo, I.,TIPS, 1982, 3: 455). In a step-down inhibitory avoidance task (0.8 mA training footshock) the pretraining injection of 1 ug/kg B-endorphin IP does not affect retrieval measured 0, 1 or 2 hr after training, but it depresses it at 6 hr; the effect is reversed by a new injection of the same dose of B-endorphin.

This type of training, like many others (Izquierdo, 1982), depletes hypothalamic B-endorphin; this effect also takes 6 hr to recover.

These findings suggest a role for B-endorphin in behavioral regulation; it could be part of a system that "marks" significant memories so that after some time they can only be properly retrieved when animals are exposed again to a situation that releases brain B-endorphin.

The effect of (inhibitory avoidance) training on hypothalamic B-endorphin is unaffected by adrenal medullectomy or chronic dexamethasone; therefore, it is not mediated by peripheral epinephrine or ACTH. It is, however, abolished by bilateral transection of the fornix (but not by other hypothalamic deafferentations), suggesting that it is mediated by a previous activation of the hippocampo/subiculum system. Gray J.A. (The Neuropsychology of Anxiety, Clarendon, Oxford, 1982) had proposed that this is a system that registrates novelty; in fact, previous evidence has shown that the hypothalamic B-endorphin response to training is best explained as a response to novelty: it occurs every time that animals are exposed to a task for the first time, regardless of whether it is aversive or not or of the type of learning involved.

Supported by funds from FINEP and CNPq, Brazil

D-11

AMYGDALA NORADRENERGIC SYSTEM & MEMORY MODULATION: INVOLVEMENT IN THE ENHANCING EFFECT OF PERIPHERAL EPINEPHRINE. K.C. Liang, R.G. Juler* & J.L. McGaugh. Center for the Neurobio. of Learning & Memory, Univ. of Calif., Irvine, CA 92717 & Dept. of Psychol., Nat'l Taiwan Univ., Taipei, Taiwan, ROC

Evidence indicates that post-trial systemic injections of epinephrine (E) enhance retention of learned responses and alter the forebrain norepinephrine (NE) levels. In view of our recent findings that the amygdala (Amyg) is involved in the memory modulatory effect of peripheral E, we investigated the interaction between the Amyg NE system and peripheral E in modulating memory processes.

Male Sprague-Dawley rats with cannulae implanted bilaterally into the Amyg were trained on a step-through inhibitory avoidance task (0.7 mA/1.0 s footshock unless otherwise noted). Retention was tested 24 hrs later. In Exp.1, rats received bilateral intra-Amyg injections of NE or vehicle (Veh) (1 µl per side). Posttraining intra-Amyg injections of 0.1 or 0.3 µg NE enhanced retention ($p<0.02$, 0.05*; respectively), while higher doses of NE had no effect. Intra-Amyg injections of 0.2 µg NE enhanced retention ($p<0.02$) if given immediately after training, but had no effect if given 3 hrs later. Further, propranolol (Prop) injected concurrently with NE into the Amyg blocked the NE enhancing effect (0.2 µg NE vs 0.2 µg NE + 0.2 or 1.0 µg Prop $p<0.02$,0.05; respectively). In Exp.2, adrenal sham operated (Sham) and demedullated (ADMX) rats were trained on 1.0 mA/1.0 s footshock and injected with 0.2 µg NE or Veh into the Amyg immediately after training. As found previously, adrenal demedullation impaired retention in the implanted rats given Veh (ADMX/Veh vs Sham/Veh $p<0.05$). However, intra-Amyg injections of 0.2 µg NE attenuated this retention deficit (ADMX/Veh vs ADMX/NE $p<0.05$). In Exp.3, immdiately after training, rats received first an intra-Amyg injection of 0.2 µg Prop or Veh and then a s.c. injection of 0.1 mg/kg E or saline (Sal). While E enhanced retention in rats given intra-Amyg Veh (E/Veh vs Sal/Veh $p<0.02$), it had no effect on rats given intra-Amyg Prop. Thus, intra-Amyg Prop blocked the memory enhancement induced by peripheral E.

These findings, taken together, are consistent with a hypothesis that the Amyg NE system may be involved in the memory modulatory effect of peripherally administered E. *Statistics are based on two-tailed Mann-Whitney U-tests.

The present study is supported by USPHS Research Grants MH12526 and AG00538 (to JLMcG).

DES-GLY VASOPRESSIN (DGAVP) FACILITATES ACQUISITION OF AUTOSHAPED OPERANT AND ADJUNCTIVE BEHAVIORS AT TWO LEVELS OF TASK DIFFICULTY. R.B. Messing and S.B. Sparber. Dept. of Pharmacology, Med. Schl., Univ. of Minnesota, Mpls, MN 55455

It has been proposed that vasopressin and its analogs exert a specific enhancing effect on learning and memory. However, recent studies using appetitive tasks have found enhancing and impairing effects of vasopressin, and results have been attributed to its aversive properties, possibly mediated by peripheral pressor receptors. DGAVP is an analog that is virtually devoid of endocrine and pressor activity, without demonstrated (in contrast to vasopressin) locomotor or aversive effects. We have shown that DGAVP facilitates the already rapid acquisition of a simple autoshaped response as well as inducing acquisition of interim adjunctive (nose-poking) behavior in Sprague Dawley rats (Eur. J. Pharmacol. 1983, 89: 43). We now show this effect in another strain of rats (Long Evans) and demonstrate more robust effects when task difficulty is increased. Further, facilitation is not due to state dependency, or to other transient effects of DGAVP on performance.

Rats were tested for acquisition of a discrete trial, food reinforced autoshaped lever touch response, in which interim retracted lever contacts (nose-pokes) and rearing activity were simultaneously monitored. In the first experiment, food pellet reinforcement occurred simultaneously with retraction of a lever which was inserted on a 45 sec random time schedule. Lever retraction occurred either when the animal touched it, or after 15 sec. Rats were given s.c. injections of saline or DGAVP 1 hr before the first 2 of 3 sessions. DGAVP (15 µg/kg) increased the rate of acquisition of the extended lever touch response, and induced increased intertrial (adjunctive) nose-poking in the third session. In the second experiment, a 6 sec delay was interposed between lever retraction and food delivery, and rats were treated with saline or 15 µg/kg of DGAVP 1 hr before the first 6 of 8 sessions. Again, DGAVP facilitated acquisition of the extended lever touch operant, and also induced an increase in rates of nose-poking in intertrial, but not in reinforcement delay, intervals, in later sessions. In both experiments, DGAVP treatment was terminated before asymptotic levels of performance were attained, yet facilitation of acquisition continued in treated groups, suggesting a specific enhancement of learning and/or enhanced memory retrieval.

Supported by Mid-Career Development Award 5K07 ES00123 to RBM and SMF-396-84 from the Minnesota Medical Foundation.

FACILITATION OF RETRIEVAL FOLLOWING PRE-TEST ADMINISTRATION OF PIRENPERONE IN MICE. H.J. Normile and H.J. Altman. Lafayette Clinic, 951 E. Lafayette, Detroit, MI 48207

There is evidence indicating that serotonin (5-HT) plays a significant role in the processing of information by the brain. Although the behavioral effects are often dependent on a number of factors, it generally appears that acute stimulation of 5-HTergic neurotransmission interferes, while disruption facilitates performance on a variety of learning and memory tasks. However, the results are not entirely consistent and often susceptable to a number of methological criticisms. Moreover, attention has generally focused on events on/or about the time of training. The following series of experiments were designed, therefore, to determine what effects a 5-HT antagonist might have on memory retrieval in Swiss-Webster mice. The 5-HT antagonist used was pirenperone (PIREN) a highly selective 5-HT type-2 receptor antagonist with little to no agonist activity. The behavioral task used was a modification of the standard thirst motivated one-trial inhibitory avoidance task (Quartermain and Altman, 1982). All injections were made prior to the retention test. In Experiments 1 and 2, dose- and time-dependent relationships were established. In Experiment 3, an attempt was made to block the PIREN induced facilitation of retrieval using 5-HT agonists and a variety of antagonists of other neurotransmitter systems. Peripheral administration of PIREN (1.0 mg/kg) 30 min. prior to the retention test results in a significant enhancement of memory. The facilitation was both time - and dose - dependent and could not be attributed to non-specific effects of the drug on behavior in general since the latencies of an independent group of non-contigently shocked animals were not significantly different from saline injected controls. The facilitation induced by PIREN could not be antagonized by any of the agonists or antagonists examined except the alpha-adrenergic antagonist phenoxybenzamine. While failing to reach statistical significance there was, however, a clear trend towards an antagonism of PIREN following haloperidol, scopolamine and bicuculline. The results confirm and extend earlier observations indicating an involvement of 5-HT in memory and suggest that interactions with other neurotransmitter systems may underlie its effects on such behavior.

ROLE OF ALPHA- AND BETA-ADRENERGIC RECEPTORS IN LEARNING AND MEMORY IN MICE. G.D. Novack, D.B. Sternberg and J.L. McGaugh. Center for the Neurobiology of Learning and Memory and Department of Psychobiology, University of California, Irvine, CA 92717

Adrenergic agonists, both endogenously released and exogenously administered, have been found to enhance learning and memory. Previous research in this laboratory and others has shown both a peripheral and central role for this modulation. In an effort to classify pharmacologically the receptors involved, we evaluated the effect of various adrenergic antagonists on performance in a one-trial learning inhibitory-avoidance task in mice. Male CFW adult mice, 22-33g, were acclimated to the housing conditions for 1 week or more. Mice were weighed, marked, and trained in a two-chambered apparatus. After moving from a lighted to a dark area, mice received a 750 μA shock for 2 sec. Antagonists were administered i.p. immediately following the training trial in doses which elicit a systemic blockade. They were returned to home cages, and 24 hr later, tested in the same apparatus. A 300 sec cutoff was used on the testing day. All antagonists used block both peripherally and centrally. Preliminary results follow:

Antagonist	Receptors	Dose (mg/kg)	Effect on Performance	Dose-related
Prazosin	a-1	0.1- 1.0	Attenuation	+
Yohimbine	a-2	0.3- 3.0	Mild Attenuation	-
Phentolamine	a-1/a-2	1.0-10.0	Mild Facilitation	±
Propranolol	b-1/b-2	1.0-10.0	Attenuation	+

The attenuation of retention by adrenergic antagonists suggests a role for adrenergic agonists in learning and memory. The clear-cut dose-relationship of the effects of propranolol and prazosin suggests an involvement of a-1 and b-1/b-2 receptors. As the effects of the a-2, and mixed alpha-antagonists were mild and not clearly dose-related, the degree of involvement of these receptors is less clear.

Supported in part by USPHS Grants AG00538 and MH12526 (to JLMcG).

AMNESIA PRODUCED BY ANISOMYCIN IN AN APPETITIVE TASK IS NOT DUE TO LEARNED AVERSION. T.A. Patterson, M.R. Rosenzweig, and E.L. Bennett. Department of Psychology, University of California, Berkeley, CA 94720.

It has been suggested that amnesia produced by protein synthesis inhibitors in appetitive tasks is due to learned aversion to the positive stimulus (Booth & Simpson, 1974). This study attempted to dissociate the effects of aversion and amnesia in an appetitive task in mice.

In experiment 1, male CD-1 mice were water deprived and trained to find water in a Y-maze. 15 min before training all groups were injected with anisomycin (ANI) (30 mg/kg). Animals were removed immediately upon leaving the arm containing the water (one-trial group), or 2 min after finding the water. Two and 4 hr later the mice received further injections of either saline (ANI-SAL-SAL) or ANI (ANI-ANI-ANI). All groups showed significant retention when tested at one day. When tested at 2 days, ANI-ANI-ANI mice receiving one-trial training were amnesic, while all other groups showed significant retention. All groups showed similar increases in water consumption in the maze at test, indicating no aversiveness of the ANI treatment.

If sickness aversion were the cause of the apparent amnesia due to the ANI, then a substance known to produce sickness aversion should produce similar results. In experiment 2, mice were given either one-trial or 2 min training, then injected with SAL or lithium chloride (LC) (150 mg/kg). Both LC groups tested at 1 day showed significant avoidance and reduced water intake. When tested at 2 days, both LC groups showed some avoidance, with a significant reduction in water intake. SAL injected mice showed significant retention and increased water consumption on both test days.

These results provide evidence for a protein synthesis-dependent phase of memory formation and evidence against a learned aversion interpretation of this finding. We suggest that the amnesia produced by ANI is due to the disruption of formation of long-term memory and not to avoidance of a stimulus that has been made aversive.

Supported by NIMH grant 1-RO1-MH36042-01A1.

PSYCHOPHARMACOLOGICAL DISSOCIATION OF MEMORY AND ATTENTION. D.M. Warburton and K. Wesnes. Dept. of Psychology, Univ. Reading, Reading, RG6 2AL, United Kingdom.

Attempts have been made for a number of years to use chemical agents as tools in the analysis of the basic neurochemical mechanisms underlying attention and memory. Although a variety of pharmacological agents have been used, a major problem has been the lack of specificity of their neurochemical action which has prevented strong inferences being made.

Recently, we have been testing human volunteers with nicotine (n=36), scopolamine (n=12) and RU 24722 (n=30) with a rapid visual information processing test to assess attention and nicotine (n=40) and RU 24722 (n=30) with memory tests. Nicotine and scopolamine have predominantly cholinergic action and RU 24722 is predominantly a noradrenergic agent, although there was some evidence for RU 24722 enhancing protein synthesis as well.

Nicotine significacantly improved attention (Wesnes, K., Warburton, D.M., and Matz, B., Neuropsychobiol., 9: 41, 1983) and scopolamine significantly impaired attention (Wesnes, K., and Warburton, D.M., Neuropsychobiol., 9: 154, 1983), but RU 24722 but had no significant effect on attention. In the memory tests, RU 24722 significantly improved free recall and nicotine significantly improved both free recall and recognition memory. Thus there was clear evidence of a dissociation with RU 24722 whereby the compound improved memory but not attention.

Use of a state dependent design in the nicotine study, showed that the effects of the cholinergic agent on memory was due both to a facilitatory effects on the input of information of information to storage, and to a direct effect on memory.

These studies support the hypothesis of a cholinergic system which controls attention and gives evidence for the idea that there is both a cholinergic and a noradrenergic system involved in human memory storage.

HABIT FORMATION IN INFANT RHESUS MONKEYS: SEX-DEPENDENT EFFECTS OF INFERIOR TEMPORAL LESIONS. Jocelyne Bachevalier and Mortimer Mishkin. Lab. Neuropsychol., NIMH, Bethesda, MD 20205.

We reported earlier that although the system underlying visual habit formation develops early in infancy, neonatal damage to an important part of this system, namely inferior temporal cortex or area TE, yields marked sparing of the function (Bachevalier et al., Soc. Neurosc., 9:26, 1983). This apparent contradiction of the notion that functional sparing occurs only if the tissue damaged neonatally is functionally immature has been resolved with the discovery that the ontogenetic development of habit formation is sexually dimorphic.

Area TE was removed bilaterally in six newborn monkeys and six adult monkeys (3 males and 3 females in each case). Twelve unoperated infants (6 males and 6 females), matched for age, and ten unoperated adults (7 males and 3 females) served as controls. Effects of surgery on habit formation were assessed postoperatively at the age of 3 months in infant monkeys and after a 15-day recovery period in adults. All animals were trained to discriminate 20 pairs of objects, the entire set being presented once every 24 hours, until they met the criterion of 90 correct responses in 100 trials. They were then trained in the same way on a second set. Whereas normal adults, both male and female, learned the first set in an average of 10 sessions, only the normal female infants learned as quickly, averaging 13 sessions. The normal male infants, by contrast, required an average of 22 sessions. Conversely, whereas TE lesions in adulthood impaired the learning of male and female animals equally ($\bar{X}$=28 sessions in each case), neonatal TE lesions impaired the learning of female infants only ($\bar{X}$=47 sessions). By contrast, the operated male infants ($\bar{X}$=24 sessions) did not differ from the normal male infants. The same pattern of results was obtained on the second set, despite a striking improvement in the scores of all infants, normal and operated alike.

Damage to area TE in infancy affects females more than males presumably because at that age area TE is more fully developed in females than in males. These results, indicative of sexual dimorphism in development of the system underlying habit formation, preserve the rule that neonatal lesions spare function only to the extent that the tissue damaged does not yet serve that function.

E-2

BEHAVIORAL AND NEUROCHEMICAL CHARACTERIZATION OF THE EFFECTS OF NUCLEUS BASALIS OF MEYNERT LESIONS IN RATS. R. F. Berman[1], R. D. Crosland[2], D. J. Jenden[2] & H. J. Altman[3], [1]Dept. Psychology, Wayne State Univ., Detroit, MI 48202, [2]Dept. Pharmacology & Brain Research Institute, UCLA, Los Angeles, CA 90024, [3]Lafayette Clinic, Detroit, MI 48207.

Loss of cholinergic function has been linked to cognitive deficits, including impaired memory and learning. Consistent with this view is the observation that destruction of the cells of origin of the major cholinergic projection to the forebrain (i.e., nucleus basalis of Meynert, NbM) in rats reduces neocortical levels of cholinergic markers (Choline acetyltransferase, CAT, and acetylcholinesterase, AChE) and impairs retention of shock-avoidance training. In the present series of studies we have further characterized the behavioral and neurochemical effects of neurotoxin lesions of the NbM. Young, male, Sprague-Dawley rats were lesioned by bilateral injection of the neurotoxin Ibotenic acid (7.5 ug/0.5 ul) into the NbM. Sham-operated and vehicle-injected animals were used as controls. Groups of lesioned and control rats were then either trained in one of two learning tasks (inhibitory shock avoidance or 14-arm T-maze) or were sacrificed at one of 4 time points (3 days, 6 days, 2 weeks or 12 weeks post-lesioning) for neurochemical evaluation. Ibotenic acid lesions of the NbM reduced cortical CAT activity by 13% at 3 days, 20% at 6 days and 30% at 2 weeks post-lesioning compared to sham-operated and vehicle-injected controls. At 12 weeks after lesioning CAT activity was still reduced by 24% compared to controls. Lesioned animals also showed impaired memory for inhibitory shock avoidance training when tested 6 days, 2 weeks or 12 weeks after lesioning indicating sustained behavioral and neurochemical effects following NbM lesions. Attempts to markedly reverse or reduce the behavioral deficits with peripheral injections of one of several doses of the potent cholinomimetic oxotremorine either immediately after training or 30 min before retention testing were unsuccessful. Similar lesions of the diagonal band of Broca (DBB) of medial septum (MS) failed to interfere with shock avoidance learning. Old rats (i.e., 24 months) showed significant impairment in both shock avoidance learning and in acquisition of a complex 14-arm sequential T-maze. Lesions of the NbM, DBB or MS failed to interfere with learning of this task. These results indicate that while old rats showed impairment in both shock avoidance and maze learning, NbM lesioned rats were only impaired in the shock avoidance task. Peripherally administered oxotremorine did not appear to be an effective strategy for reversing the behavioral deficits of NbM lesions. Considerable specificity of task and brain region appear to exist with respect to involvement of the cholinergic system in memory. (Supported by NIA AGNS07351 and the Wayne State Univ. Neuroscience Program).

E-3

THE AMYGDALOID INVOLVEMENT IN THE ACQUISITION OF TASTE POTENTIATED ODOR AVERSION LEARNING. F. Bermudez-Rattoni, C.V. Grijalva, and J. Garcia. Mental Retardation Research Center, Psychology Department, University of California, Los Angeles, and Centro de Investigaciones en Fisiologia Celular, UNAM.

We have shown that odor and taste stimuli may be affected by different temporal parameters during flavor aversion conditioning. Odor must be followed immediately by illness, however, when odor plus taste is followed by delayed illness, odor becomes aversive as if it has been potentiated by taste.

In testing a neural model for the potentiation of odor by taste (Garcia et al., 1984) it was shown that "reversible lesions" of the amygdaloid complex (using procaine) disrupts potentiation odor aversions, but not taste aversions. In the present experiment the role of the amygdaloid complex and its specific nuclei was tested in the conditioning of potentiated odor by taste aversions. In one experiment two groups of rats were given large electrolytic lesions in the amygdala including central, medial, cortical, basolateral and lateral nuclei (AMX) or sham operations (SH). In a second experiment, another 4 groups of rats received either same electrolytic lesions in the medial and basomedial nuclei (M), central nuclei (C), lateral and basolateral nuclei (L), sham operations (SH). Following postoperative recovery each group received acquisition of odor-taste compound aversions. The acquisition was done by following the stimuli compound presentation with delayed illness. Almond odor and .1% saccharin were the conditioned stimuli while the unconditioned stimuli were 190 mg/kg of lithium chloride, i.g.

After conditioning in the first experiment, tests with odor and taste alone showed that the SH group developed strong taste and odor aversions, however amygdaloid lesions (Group AMX) completely blocked both odor and taste aversions. In the second experiment, the tests showed that all the groups had strong taste and odor aversions, except Group (L) which showed a significant disruption of odor aversions ($p < 0.05$) compared to the sham control group. However, all groups including Group L, exhibited strong taste averions.

In conclusion, this data showed that the amygdala is involved in the gating of odor by taste, since the large amygdaloid lesions produced complete blocking of odor and taste aversions. Moreover it is suggested that, the lateral and/or basolateral nuclei are particularly involved in the process by which the odor is indexed into the visceral system.

E-4

PLASTICITY OF SUBSTANTIA NIGRA PROJECTIONS AND THEIR RELATIONSHIP TO BEHAVIOR. J.P. Huston, S. Morgan and H. Steiner. Inst. of Psychology III, Univ. of Düsseldorf, 4000 Düsseldorf, F.R.G.

In a series of experiments we examined the effect of experimentally-induced turning on crossed efferents from the substantia nigra (sn). Initially turning behavior was induced by a central lesion; (a) hemidetelencephalization, (b) injection of either kainic acid or 6-hydroxydopamine into the sn on one side. About 1 week after any of these lesions we found an increase in crossed projections from the sn contralateral to the turning direction to the contralateral thalamus and caudate nucleus. These connections were demonstrated either by the retrograde transport of horseradish peroxidase or fluorescent tracers. The appearance of these connections coincided, in time, with compensation for the lesion induced turning. Prevention of the turning behavior resulted in a suppression of the appearance of these connections and the behavioral compensation. From this result we concluded that the relationship between the appearance of these connections and the behavioral compensation is not fortuitous.

We then looked at whether turning behavior, in the absence of a central lesion, would result in the appearance of these connections. We induced turning behavior by denervation of the fore- and hind limbs on one side. We found that this resulted in turning behavior which decreased over time. The decrease in turning behavior was associated with an increase in crossed nigro-thalamic projections ipsilateral, but not contralateral (as shown by horseradish peroxidase uptake), to the peripheral lesion.

We then investigated whether asymmetrical behavior, in the absence of any lesion, is related to these connections. We induced turning behavior in normal rats, by amphetamine (1 mg/kg). We then looked at the nigro-caudate projections, utilizing the retrograde transport of HRP. Our results showed that there is a relationship between the direction of amphetamine induced turning and the nigro-caudate projections.

E-5

PASSIVE AVOIDANCE LEARNING AND MEMORY STORAGE IN DECEREBRATE RATS. C. Tomaz and J.P. Huston. Institute of Psychology III, University of Dusseldorf, Federal Republic of Germany.

The aim of the present study was to determine if "hypothalamic rats" are able to learn a passive avoidance response and in the positive case, whether memory for this response is stored at the subtelencephalic level. "Hypothalamic rat" refers to a preparation in which the neocortex, hippocampus, amygdala, septum, striatum and the major portions of the thalamus have been bilaterally ablated by aspiration; i.e. the hypothalamus is the only forebrain structure left intact. The passive avoidance response that we used was the uphill avoidance task. In this task the animal is placed on a slanted platform with the head pointing downhill. When the animal turns around to climb up the platform it receives a tailshock. In the first experiment (learning) the animals were tested 24 hours after decerebration. Control animals received tailshock which was non-contingent on the uphill response or they received no tailshock. The experimental rats exhibited retention of the passive avoidance learning when tested 2, 8 and 24 hours after the training. In the second experiment (memory) the animals received tailshock contingent on the uphill response, no tailshock or non-contingent shock. Eight hours after training they were operated or sham-operated. Twenty-four hours after the operation 10 repeated measurements were carried out with an interval of 5 min between them. The experimental animals exhibited retention of the passive avoidance learning indicating memory storage of this task independent of the ablated structures.

INTERRUPTION OF PROJECTIONS FROM THE MEDIAL GENICULATE NUCLEUS TO AN ARCHI-NEOSTRIATAL FIELD DISRUPTS AUDITORY FEAR CONDITIONING. J.E. LeDoux, A. Sakaguchi, J. Iwata, and D.J. Reis, Lab. Neurobiol. Cornell U. Med. Coll. NY, NY 10021

Auditory fear conditioning in rats is abolished by lesions of the inferior colliculus and medial geniculate (MG) but not of auditory cortex (LeDoux et al, J. Neurosci. 4: 683-696, 1984). Projections from MG to subcortical rather than cortical targets thus appear to mediate auditory fear conditioning. Since MG projects to a striatal field (STR) involving the posterior neostriatum (caudate-putamen) and the underlying dorsal archistriatum (central and lateral nuclei of the amygdala) (LeDoux et al, Neurosci. Abs., 1984), we have sought to determine whether interruption of these projections disrupts conditioning.

Lesions were placed unilaterally in MG and in the contralateral (n=15) or ipsilateral STR (n=6). Controls were unoperated (n=8), received unilateral MG lesion alone (n=6), or received unilateral MG lesion in combination with the contralateral anterior neostriatum (n=4) or ventromedial hypothalamus (VMH, n=6). After 14 days the animals were classically conditioned (conditioned stimulus, CS: 800 Hz, 82 db, 10 sec pure tone; unconditioed stimulus (US): 2.0 mA, 0.5 sec, d.c.) and implanted with an arterial cannula for recording mean arterial pressure (MAP). Increases in MAP and the suppression of exploratory activity (as indicated by the duration of freezing) by the CS were measured.

The CS elicited elevations in MAP (16±3 mmHg) and induced freezing (90±15 sec) in unoperated controls. Unilateral lesions of MG alone did not affect the MAP or freezing responses. Lesions of MG and the contralateral STR reduced MAP by 67±1% ($p<.01$) and freezing by 68±1% ($p<.01$). Lesions involving the neostriatal and archistriatal aspects of STR had the same effects. Lesions of MG and the ipsilateral STR had no effect. Unilateral lesion of MG in combination with the contralateral VMH or anterior neostriatum did not affect responses.

These findings demonstrate that in the absence of direct ipsilateral connections linking MG to STR, auditory fear conditioning does not take place. We conclude that auditory fear conditioning is mediated by projections from MG to the posterior caudate-putamen and/or dorsal amygdala. Supported by PHS grant HL 18974.

DISSOCIATION OF NEURAL REGIONS NECESSARY FOR ALPHA AND CONDITIONED RESPONSES TO A VISUAL STIMULUS. R.W.Skelton, M.D. Mauk & R.F.Thompson. Psychology Dept., Stanford, CA 94305.

Situations in which classical conditioning procedures result in the augmentation of a pre-existing response to the CS have been termed alpha conditioning to distinguish them from situations where responses develop de novo. Historically, the implicit assumption has been that different neural mechanisms may mediate these two apparently different situations. Eyeblink conditioning in the rabbit using auditory CSs is an example where CRs develop de novo. However, using light from an incandescent bulb as a CS, we have observed alpha responses in this paradigm. When paired with a corneal airpuff US the responses to the light increased; an instance of alpha conditioning.

The dentate-interpositus (DI) region of the cerebellum is known to be essential for conditioned eyeblink responses in the rabbit. We report here that small lesions in the DI do not disrupt alpha responses to a bright light but prevent acquisition of CRs to a lesser intensity light.

Sixteen albino New Zealand rabbits were prepared with EMG electrodes in the upper eyelids and with chronic lesion electrodes implanted in the cerebellum. Electrodes were aimed at the DI region in half the animals and more dorsally (in the cortex) in the rest. After two days of testing to measure alpha responses to a bright light (3V flashlight bulb, 1 cm from eye) and to establish conditioned responding to a tone CS (1 KHz, 85 dB) through paired presentation with a corneal airpuff US, lesions were made by passing 2mA anodal current for 2 minutes through the lesion electrodes. Three days were allowed for recovery. On days 1 and 6 of post-lesion testing, the alpha responses to the light and CRs to tone were evaluated. On the intervening 4 days, half the animals in each group received 117 paired presentations of a lesser intensity light (1.5V through same 3V bulb) with the airpuff US. The rest received an equal number of explicitly unpaired presentations of the same stimuli. The DI lesions abolished the conditioned responding to tone, but had no effect on the alpha responding to the bright light. Comparisons between the two lesion groups given paired presentations of the light and airpuff (i.e. DI versus cortex) showed that DI lesions prevented acquisition of conditioned responding to the light CS. These data demonstrate that a brain region essential for CRs to light is not essential for the alpha (or reflex) response to light (and tone) and suggest that the alpha and conditioned responses are subserved by different neuronal circuits even though the responses are topographically similar.

F-1

DEVELOPMENT OF THE NEURAL NETWORK CONTROLLING SONG BEHAVIOR IN ZEBRA FINCHES. S.W. Bottjer, S.L. Glaessner & A.P. Arnold. Dept. of Psychology, UCLA, CA 90024.

The primary purpose of this study was to examine the normal ontogeny of the total volume of 3 brain nuclei that have been directly implicated in song learning and behavior in male zebra finches. In addition, the corresponding nuclei of age-matched females were examined. 18 male and 12 female zebra finches were overdosed with anesthetic and perfused with saline-formalin. Brains were frozen-sectioned transversely at 25 um and stained with thionin. Alternate sections were examined using a microprojector. HVc (caudal nucleus of the ventral hyperstriatum), RA (robust nucleus of the archistriatum) and MAN (magnocellular nucleus of the anterior neostriatum) were outlined in order to calculate the total volume of each nucleus. As a control, the average cross-sectional area of the telencephalon at the level of the anterior commissure was measured. All birds were divided into 3 age groups with means of 12, 25 and 53 days. These 3 ages correspond to the time (a) prior to production of any song, (b) when song sounds are first produced, and (c) when the final song pattern begins to form. Female zebra finches do not sing at any age.

The major findings are as follows: The volumes of HVc and RA were smaller in females than in males at all ages studied. Between 12 and 25 days the volumes of female HVc and RA increased by 23 and 15%, respectively, but the telencephalic control area increased by 32%. Female HVc and RA decreased by 21 and 43%, respectively, between 25 and 53 days, whereas the control area did not change. The volume of male HVc and RA increased by 147 and 46%, respectively, between 12 and 25 days, whereas the telencephalic control area increased by only 27%. Between 25 and 53 days, male HVc and RA increased by 28 and 78%, respectively, while the control area decreased by 3%. Even more striking was that MAN had a very large volume at 25 days, which decreased (by 59%) by 53 days. Measurements of soma size and neuronal density demonstrated that the decreased volume was attributable to a loss of over 50% of the neurons in MAN between 25 and 53 days. This interval corresponds to a restricted period of development when MAN lesions disrupt song learning (Bottjer et al, Sci. '84).

These findings suggest the following: (1) the sexual dimorphism in the song-control system is evident at 12 days but increases markedly thereafter, primarily due to growth of male HVc and RA, but also to the atrophy of female HVc and RA; (2) the increase in volume in male HVc appears to lead that in RA, suggesting that hormones may act directly on HVc to trigger growth, and that HVc may then exert a trophic influence on RA; (3) MAN is large when birds are learning to produce song, and decreases markedly around the time when the motor pattern of song begins to stabilize. The loss of neurons from MAN may be attributable to cell death or re-differentiation and migration of some neurons.

F-2

METABOLIC CORRELATES OF KINDLING-INDUCED CHANGES IN THE REWARDING EFFICACY OF HIPPOCAMPAL STIMULATION: A 2-DEOXYGLUCOSE AUTORADIOGRAPHIC STUDY. K. A. Campbell. Dept. of Psych., Univ. of Pennsylvania, Phila., Pa., 19104.

Previous studies have demonstrated that the usually very slow acquisition of hippocampal (HPC) self-stimulation (8-14 daily 30-min sessions) can be greatly faciltated (to 1-3 sessions) by a prior program of HPC kindling (Brain Research, 159, 458, 1978). It has been hypothesized that the reinforcing consequences of HPC stimulation may develop as the stimulation-induced activity propagates more widely through pathways potentiated by prior kindling. The metabolic tracer [^{14}C]-2-deoxyglucose (2DG) was used to measure the functional activity resulting from electrical stimulation of the HPC, comparing uptake in a group of confirmed HPC self-stimulators with a group of stimulation-naive rats. A group of implanted, unstimulated naive controls were also used.

17 rats were implanted in the dorsolateral HPC (CA-3), of which 6 were trained to self-stimulate: optimal parameters using 0.5 sec trains of 0.1 msec square, monophasic-negative pulses were found to be 80 μA at 75/sec. During 2DG uptake (30 μCi i.p.), the confirmed self-stimulators were either allowed to self-stimulate (n=2) or given programmed stimulation (5 sec ISI; n=4) at the above optimal parameters for self-stimulation. Stimulation-naive rats were either given the same programmed HPC stimulation (n=7), or were not stimulated (n=5). After 45 min, the animal was immediately sacrificed, perfused, and the brain frozen, sliced, and prepared for autoradiography; details of preparation and computer densitometry of radiographs have been described in Gallistel et al. (Neurosci. Biobehav. Rev., 1982).

Radiographic analysis indicated that CA-3 stimulation in a confirmed self-stimulator results in widespread increases in metabolic activation throughout HPC fields CA-1,2,3 and posterior subiculum bilaterally, whether stimulation was self-administered or programmed; the dentate gyrus was unaffected. In naive rats, the programmed CA-3 stimulation produced very limited activation, in most cases restricted to the region around the electrode tip, with metabolism in contralateral or distal HPC not markedly different from unstimulated controls.

The present results demonstrate that HPC stimulation in experienced HPC self-stimulators (kindled animals) produces considerably more widespread activation of HPC than does the same HPC stimulation in naive rats which would not be expected to exhibit self-stimulation.

THE ENHANCED NEURAL RESPONSE INDUCED BY POSTNATAL OLFACTORY EXPERIENCE IN NORWAY RATS IS ODOR-SPECICIC. R. M. Coopersmith* and M. Leon. Department of Psychobiology, University of California, Irvine CA 92717.

Norway rat pups develop a preference for the odor of their mother, or an arbritrarily selected odor, based on postnatal experience. Daily exposure to peppermint odor during the first 18 days of life will induce both an attraction and an increased neuronal response in specific olfactory bulb glomeruli to peppermint odor. Since it is possible that experience with one odor enhances the glomerular response to any odor, we gave pups experience with cyclohexanone odor and then tested them on day 19 with peppermint odor.

On days 1 to 18 after birth, rat pups received exposure to either peppermint odor (peppermint-familiar) or cyclohexanone odor (cyclohexanone-familiar) from a flow-dilution olfactometer. On day 19, all pups were injected with ^{14}C-2-deoxyglucose (200 uCi/kg) and given a 45 min test exposure to peppermint in an apparatus that allowed us to analyze respiration rate and sniff frequency. We then prepared autoradiographs of olfactory bulb sections along with calibrated standards. The films were then analyzed with a computer-based image processing system which allowed quantitative comparisons between uptake sites to be made.

Peppermint-familiar pups showed enhanced activity in three laterally-located complexes of glomeruli, 1.5-2.2 mm from the rostral pole of the bulb, confirming our previous findings. The same peppermint test exposure given to cyclohexanone-familiar pups induced significantly less activity in these same glomerular areas.

The enhanced neural activity in the peppermint-familiar animals was not a result of an increased odor stimulus to the olfactory system of these pups. The overall number of respirations for both groups of pups were not different during the test, and the number of high frequency respirations characteristic of sniffing were virtually identical. We have shown that early exposure to an odor will induce an enhanced olfactory bulb response specific to that odor.

AGE DIFFERENCES IN PERFORMANCE OF RATS AND MICE IN A 14-UNIT T-MAZE. D. Ingram*, E. Spangler*, J. Freeman* and W. Richards* (SPON: M. Heft). Gerontology Research Center, NIA, NIH, Baltimore City Hospitals, Baltimore, MD 21224

In a series of studies, Goodrick (cf. J. Gerontol., 27: 353, 1972) demonstrated the effects of aging on performance of rats in a 14-unit T-maze. The task involved food deprivation over several weeks. We have altered this protocol to assess age differences in performance of rats and mice in an automated, 14-unit T-maze involving footshock escape/avoidance. Male Wistar rats and C57BL/6J mice were given preliminary training in one-way active avoidance (US=0.6 and 1.0 mA for mice and rats, respectively) in a straight runway (1 m long). The criterion was 8/10 successful avoidances (CS-US interval=10 sec) across two consecutive 10-trial daily sessions. The day after meeting this criterion, each animal was provided the first of two 10-trial sessions in the 14-unit T-maze with the second session 24-hr later. The animal was required to traverse each quadrant of the maze within 10 sec to avoid a footshock (0.6 and 1.0 mA for mice and rats, respectively). Movement of the animal through the maze is detected by a series of infrared photocells, and these data are stored in a microprocessor. All age groups demonstrated learning in this task; however, the rate of acquisition was slower and the asymptotic level of performance was higher as a function of age in both rats and mice. The mean number of errors per trial for rats 6, 12, 18, and 24 mo of age was 5.4, 7.7, 7.4, and 11.2, respectively. This age difference was significant according to a one-way ANOVA, $F(3,20) = 6.53$, $p < .01$. The mean number of errors per trial for mice 6, 12, 18, 24, and 30 mo of age was 4.7, 5.1, 6.2, 6.5, 7.4, respectively, which was also a significant age effect, $F(4,33) = 2.80$, $p < .05$. Preliminary analysis of learning strategies revealed perseverative responses at certain maze locations in all age groups but which persisted longer in older groups. Results of additional studies indicated that intact vision was not important to maze performance as different age groups could learn in the dark. Still other findings suggest that retention can be demonstrated over several weeks, but preliminary analyses suggest the existence of age differences in long-term retention. Thus, our modified complex maze protocol appears to produce reliable age differences in the performance of rats and mice.

ONTOGENY AND PLASTICITY OF EXPLORATORY BEHAVIOR AND HIPPOCAMPAL DEVELOPMENT IN RATS. E.M. Kurz, B.L. Harkins, and L. Nadel, Program in Cognitive Sciences, University of California, Irvine, CA. 92717.

The hippocampus is thought to mediate various aspects of spatial behavior in mammals, and we have hypothesized that the hippocampus is involved in exploration. In rats, the hippocampus undergoes extensive development through the late postnatal period and manipulations such as stress administered during this period have been shown to affect later exploratory behavior. We have examined the ontogeny of exploratory behavior and its relation to hippocampal development in infant rats following two types of early experience.

In the handled condition, litters of hooded rats were handled daily starting on postnatal day 4 (P4; P1 = day of birth) and separated from the dam for 9 hours on days P9, P11, and P13. Control rats were left undisturbed until testing began for both groups on P16. From P16 through P25 exploratory behavior was measured for half of each litter in a 6'x5' arena containing 4 objects. The remaining half of each litter was tested in running wheels to obtain an independent measure of general activity.

In general, the ontogeny of exploration was similar for handled and control rats in the arena: total time spent near the objects was initially low, followed by an abrupt increase to near-maximal levels. However, in control rats this abrupt increase typically occurred between P21 and P22, while for handled rats this increase occurred significantly earlier, between P18 and P19 ($t=3.04$, $df=34$, $p<.05$ two-tailed). The effects of early handling were especially pronounced in males ($t=2.38$, $df=16$, $p<.05$ two-tailed). These changes in exploratory behavior were not reflected in the running wheel data, suggesting that changes in levels of general activity are not responsible for the exploration effects.

To obtain an independent anatomical measure of hippocampal maturity during the period in which the behavioral changes occur, hippocampi from a separate set of pups were removed and assayed for myelin protein. This index of hippocampal development was strikingly similar in pattern and time course to the behavioral data obtained from the arena. Myelin assays from control areas of the brain (neocortex and cerebellum) did not show this change during the period we examined.

The ontogeny of exploration appears to be a step function, suggesting that some maturational threshold must be reached before exploration will be observed. This pattern is reflected in anatomical measures of hippocampal development. Furthermore, the time course of maturation of exploratory behavior can be altered by early experience.

Supported by NIH MH08911, NS 17712, and MOD 12-143.

Food storage and spatial memory in chickadees and tits. David F. Sherry, Department of Psychology, University of Toronto, Toronto, Ontario, Canada M5S 1A1

Marsh tits (Parus palustris) and black-capped chickadees (Parus atricapillus) store single food items, such as seeds and insects in widely-scattered storage sites in their winter territories and home ranges. An individual bird may store several hundred food items in a single day, and most food is recovered within a few days of storage.

Field and laboratory studies have shown that these species can accurately relocate storage sites, and use spatial memory to do so. If the birds indeed rely on spatial memory to relocate scattered caches, we might expect memory to capable of dealing with three other events that affect the status of caches. - 1) the recovery of stored food, 2) the loss of stored food to other animals, and 3) the storage of different kinds of food.

Laboratory studies with captive birds showed that marsh tits and black-capped chickadees that were allowed to recover half of their stored food on the day following storage did not, in a subsequent test one day later, revisit caches they had emptied. They did, however, relocate and visit caches they had not yet emptied. This result was obtained under conditions in which stored food had been experimentally removed from all sites, indicating that the birds were not discriminating the two classes of cache sites visually, olfactorily, or by some other means. In addition, sites where recovery had previously occurred were found not to be spatially clustered.

In a second experiment, food was experimentally removed at random from one third of caches, and the bird was allowed to discover the loss. In a subsequent test, subjects avoided returning to these cache sites, while continuing to successfully relocate other caches. Thus, the act of recovery is not necessary for the birds to distinguish,in memory,intact from previously recovered or lost caches.

In a final experiment, birds were allowed to store both safflower and sunflower seeds. Of the two, sunflower seeds are preferred, though both are cached. During a test one day following storage, the birds were able to distinguish sites were the two types of seed had been hidden, and returned more often and for longer periods to search at sites where preferred sunflower seeds had been stored.

These results indicate that in addition to retaining in memory the spatial locations of many widely scattered storage sites, food-storing birds retain in memory additional information concerning the status and contents of these caches.

F-7

OLFACTORY LEARNING IN RATS AS A MODEL FOR STUDYING MEMORY IN COMBINATORIAL CIRCUITRIES

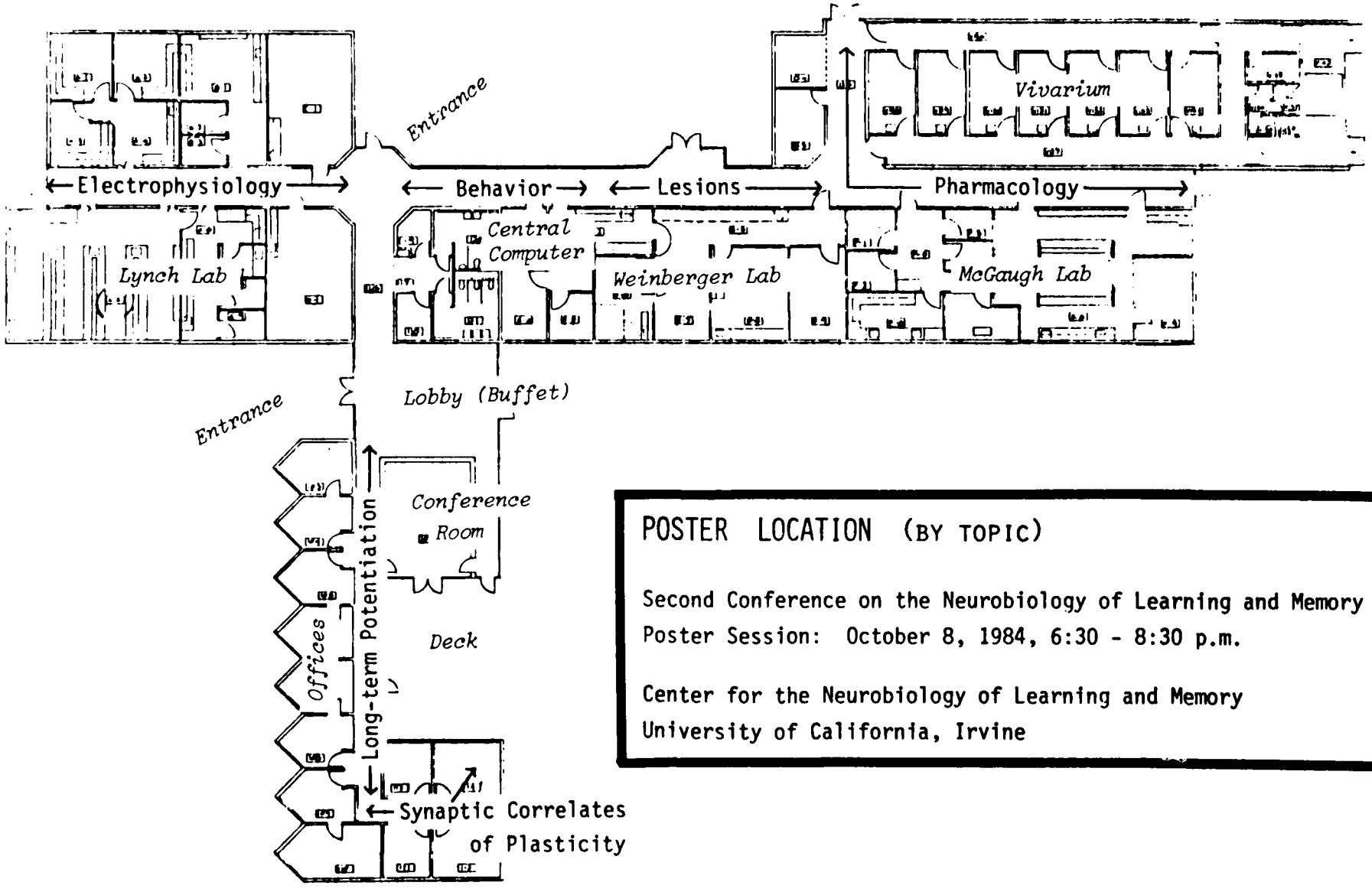
U. Staubli, D. Fraser, and G. Lynch.

Center for the Neurobiology of Learning & Memory, University of California, Irvine CA 92717

A number of theorists have argued that many aspects of human memory must represent changes in the operation of combinatorial circuitries in which individual neurons respond to near simultaneous activation of functionally (and spatially) disparate inputs.

In this poster, we will first interpret recent neuroanatomical work from several laboratories as indicating that the primary and secondary projections of the rat olfactory system are organized according to combinatorial principles. A number of behavioral predictions that follow from this analysis and attempts to test certain of these will be described. In particular, data will be presented showing that rats learn some complex odors as units and do not recognize individual components upon re-testing. These results will be integrated with those of previous lesion studies to produce a general hypothesis about the role of the hippocampus in olfactory memory and the conclusion drawn that the storage of olfactory information in rats may provide an experimentally accessible model of a type of memory processing common in human cognition.

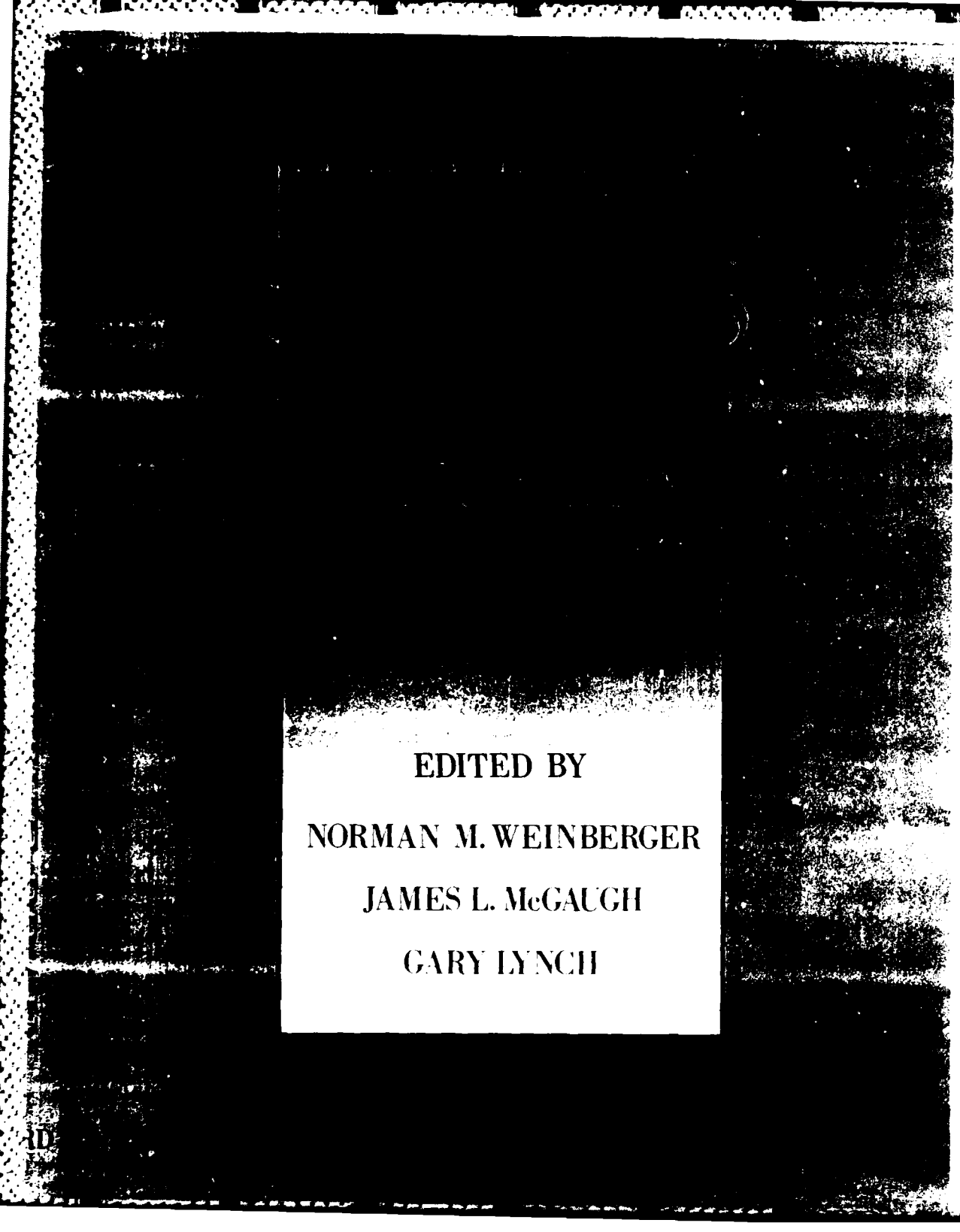
(supported by a grant from the Office of Naval Research)



POSTER LOCATION (BY TOPIC)

Second Conference on the Neurobiology of Learning and Memory
Poster Session: October 8, 1984, 6:30 - 8:30 p.m.

Center for the Neurobiology of Learning and Memory
University of California, Irvine



MEMORY SYSTEMS OF THE BRAIN

EDITED BY

NORMAN M. WEINBERGER, PH.D.,
JAMES L. MCGAUGH, PH.D.,
AND GARY LYNCH, PH.D.
University of California at Irvine

"A rich source of problems, data, and theory characterizing contemporary research aimed at one of the truly fundmental puzzles of brain science . . . the correlation between brain mechanisms and behavioral cognitive processes of learning and memory. Whole chapters have been written by people working at the cutting edges of their own subject matter areas. . . . The coverage of the volume is broad: from morphological, biomedical, and physiological changes at the cellular level, to the intricacies of the manifestations of learning and memory at the level of observable behavior, from simple invertebrates to adult humans, from field and case studies to precisely controlled experiments."
–Endel Tulving, Ph.D., F.R.S.C., University of Toronto

Investigations of neurobiological processes underlying learning and memory have generated important insights about memory systems in animals and humans. Rarely, though, have these findings been placed side by side to pose the critical question: Are all memory systems of the same form, or are there fundamental physiological differences between species? In addition to exploring current research in depth, this volume presents considerable evidence suggesting that there may be many forms of learning and memory, possibly based on different neuronal systems.

MEMORY SYSTEMS OF THE BRAIN applies the insights gained from animal studies to an understanding of the learning process in the human brain. The daunting complexity of the task—learning how the brain acquires and stores experience—demands inquiry on levels ranging from molecular biology to behavioral ecology, and the distinguished contributors to this volume show a remarkable ability to draw on these disciplines. Divided into three sections, the book begins with analyses of memory systems in specific organisms, proceeds to comparative studies of learning, and concludes with a series of illuminating juxtapositions of human and animal studies. The chapters in each section are followed by commentaries and critiques that fit their conclusions into the context of other research.

For the researcher and advanced student in any aspect of neuroscience and cognitive science, this cohesive, comprehensive volume is an essential collection of current ideas about the mechanisms of the brain that control memory.

This work relates to Department of Navy Grant N00014-84-G-0108 issued by the Office of Naval Research. The United States Government has a royalty-free license throughout the world in all copyrightable material contained herein.

Library of Congress Cataloging in Publication Data

Main entry under title:

Memory systems of the brain.

Papers from the Second Conference on the Neurobiology of Learning and Memory, held Oct. 6-9, 1984, at Irvine, Calif. and organized by the Center for the Neurobiology of Learning and Memory.
Includes bibliographies and indexes.
1. Memory—Physiological aspects—Congresses.
2. Learning—Physiological aspects—Congresses.
3. Cognition—Physiological aspects—Congresses.
I. Weinberger, Norman M. II. McGaugh, James L.
III. Lynch, Gary IV. University of California, Irvine. Center for the Neurobiology of Learning and Memory.
V. Conference on the Neurobiology of Learning and Memory (2nd : 1984 : Irvine, Calif.)
QP406.M46 1985 153.1'2 85-24756
ISBN 0-89862-666-8

ACKNOWLEDGMENTS

The conference on which this book is based was supported by a number of organizations including the University of California, Irvine; the Office of Naval Research; the Air Force Office of Scientific Research; Monsanto Company; Allergan Pharmaceuticals, Inc.; Health Resources Corporation of America; and The Irvine Company. We would also like to acknowledge and thank Lynn Brown, Nan Collett, Rita Stephens, and Jacqueline Weinberger for their meticulous and dedicated help in planning and coordinating the conference and for their efforts to assure the timely completion of this book. We are pleased to acknowledge the indexing labors of David Lane for the subject index, Lisa Weinberger for the author index, and Robert Finn for invaluable advice and assistance.

PREFACE

Brains reasonably may be considered to be information processing systems, which acquire, store, and manipulate information in the service of adaptive behavior. Accordingly, learning and memory (i.e., acquisition and storage, respectively) are critical and central topics in neurobiology. A greatly increasing volume of research on learning and memory is a significant characteristic of current biological and behavioral approaches. There is ample reason to believe that this trend will continue because of the many advances that have emerged from recent studies relating learning and memory to their neural substrates, on the one hand, and placing them within their evolutionary and ecological contexts, on the other hand.

This volume is a product of the Second Conference on the Neurobiology of Learning and Memory, which was held at Irvine, California, October 6–9, 1984, and organized by the Center for the Neurobiology of Learning and Memory. Its focus differs from the previous volume that grew out of the first Irvine conference, marking the inauguration of the Center. That book (Lynch, McGaugh, & Weinberger, 1984) was more concerned with recent advances in cellular and brain system mechanisms and modulators and less concerned with relating findings from animal studies to human memory. Both volumes are concerned with presenting concepts and findings that characterize current research, organized on the basis of enduring problems and themes. As in the case of the previous monograph, this book is divided into major sections, each of which contains main chapters followed by directed comments and critiques. Its broad scope is intended to reflect some of the varied lines of inquiry into learning and memory, each of which has a rich primary source literature. The bibliographies provide a sense of this literature as well as focal points of entry for the reader who wants to embark on a more detailed journey into an area of interest.

Following an introductory chapter, the book begins with consideration of cellular- and systems-level mechanisms in diverse organisms and neural substrates. Not surprisingly, the mammalian hippocampus receives much attention, reflecting a current major focus of research. The second section concerns learning and memory from a comparative point of view. This section reflects increasing concern with delineating learning and memory characteristics and capacities in settings appropriate to the subject's ecological niche as well as other issues concerning beliefs about what is learned and the prospects for developing general process theories of learning. The final

section juxtaposes human and animal studies of learning and memory, bringing similarities and differences into the same arena for direct comparison. This final section also places some emphasis upon a thread that runs thoughout the fabric of the book as it did in animated discussions during the Conference: Is there more than one form of memory, and just how is this issue to be settled?

An important point that emerged from the Conference, and which we hope is adequately reflected in the book, is that understanding how the brain acquires and stores experience constitutes a very central and complex task of very large proportions. It requires inquiry at several levels, from the molecular to that of behavioral ecology, as well as ways of bridging these levels. Of equal importance, and perhaps of greater difficulty, are the conceptual problems. In this regard, implicit assumptions should be made explicit so that they can be addressed directly. Furthermore, it is essential to realize that the need for conceptual advances is not relaxed by the gathering of new data, but on the contrary, becomes more urgent.

REFERENCE

Lynch, G., McGaugh, J. L., & Weinberger, N. M. (Eds.). *Neurobiology of learning and memory*. New York: Guilford Press, 1984.

CONTENTS

Introduction

Norman M. Weinberger
James L. McGaugh
Gary Lynch
University of California, Irvine

This volume is divided into three sections: Brain Systems and Learning; Comparative Aspects of Learning and Memory; and Learning, Memory, and Cognitive Processes. Each section begins with chapters on selected topics and ends with critical commentaries. The inclusion of these commentaries reflects the need to examine the assumptions and approaches of all lines of inquiry, not merely those that are included in this volume.

Despite the breadth of topics and the variety of approaches, certain themes are common to the entire volume. These include whether memory is unitary or has multiple forms, the degree to which learning mechanisms have been conserved in evolution, the sense in which human memory is qualitatively different from that of other animals, and the nature of what is actually learned and how it is represented in brains.

BRAIN SYSTEMS AND LEARNING

The first section concerning neural systems deals with substrates of learning and memory. It addresses several important issues, including the nature of relevant cellular mechanisms, loci of learning-induced plasticity within the nervous system, and the role of the hippocampus, and long-term plasticity within the hippocampus, in memory.

Dominant theories have assumed that learning requires synaptic change. However, the impressive analysis of classical conditioning in *Hermissenda* by Alkon and his associates reveals changes in calcium-dependent potassium channels rather than direct changes in synaptic function. The locus of change is at the extreme periphery, in the photoreceptor itself, which receives convergent input from the conditioned visual and unconditioned vestibular stimuli. This biophysical change is reported to occur also in the hippocampus of the rabbit during classical conditioning, a finding suggesting an evolu-

tionary conservation of mechanism despite vast differences between gastropod and mammalian brains.

Plasticity in the sensory system of the conditioned stimulus also develops in the pigeon, as delineated in the extensive studies of David Cohen. Here the plasticity is seen not in the photoreceptors but in the avian "equivalent" of the lateral geniculate nucleus. This might suggest phylogenetic encephalization of plastic loci within the sensory system of the conditioned stimulus. Cohen also points out that multiple sites of plasticity may develop somewhat independently even within the same general circuitry for a particular conditioned response, a finding that argues against strict localization of a memory trace.

Neural plasticity that accompanies learning is, in any event, not restricted to sensory systems. Barnes and McNaughton argue that place learning involves the selective distribution of changes in synaptic strength in the hippocampus of the rat; furthermore, the storage of information is said to correspond to this distribution. This conclusion is based upon the use of high-frequency stimulation of selected hippocampal paths to produce "long-term enhancement" of transmission in a wide variety of circumstances. However, they conclude that the hippocampus need not be viewed as a site of permanent storage of spatial information, but rather may be a shorter term store upon which the neocortex draws information.

Although long-term enhancement/potentiation within the hippocampus is proving to be an important tool in the study of mechanisms of memory, it may not be a simpler model process than is experience-induced learning. Abraham and Goddard point out that electrical stimulation within the hippocampal formation, which causes "long-term potentiation," actually produces at least four long-term effects or traces. Although it would be premature to conclude that each of these physiological effects is isomorphic with a separate memory of the type associated with an environmental event, these findings do demonstrate that a neural substrate is capable of establishing multiple, independent traces. This is consistent with the view that multiple memories are formed during a behavioral learning episode. Direct behavioral evidence supporting this view is provided by Rescorla and also by Mackintosh in Sections II and III, respectively.

Given Alkon's findings, it might be thought that hippocampal long-term potentiation might involve changes in membrane channels. However, Greenough's findings indicate that morphological synaptic changes are involved. He also presents several pieces of evidence to support the idea that synapses are formed in the neocortex of rats during learning experiences. At the same time, Greenough indicates the additional criteria that need to be met to conclude that learning does cause the formation of new synapses. Even though it might appear that "synapses on demand" are in conflict with the role of channels in plasticity, Greenough notes that different mechanisms for plasticity may be related to the very different durations of various memories. Here again, the issue of multiple memory mechanisms is evident.

In commentary, Ashe points out that mechanisms of cellular plasticity also involve an enabling and enhancing role for catecholamines. It is particularly noteworthy that some of the synaptically mediated effects demonstrated have a time course orders of magnitude longer than the textbook descriptions of synaptic potentials. Moreover, Ashe has extended these findings from the superior cervical ganglion to the hippocampus, thus suggesting an evolutionarily conserved process. Wenzel and Matthies present additional strong evidence that long-term potentiation critically involves the formation, or perhaps uncovering, of synapses in the hippocampus. Deadwyler provides a comprehensive study of how potentials evoked by hippocampal stimulation are altered during a behavioral learning situation. His findings suggest that the hippocampus acts like a limited capacity buffer that can hold the results of recent experiences. Berger and Sclabassi argue that the analysis of hippocampal or other circuits requires nonlinear systems analysis because of the involved complexity. Applying this analysis to long-term potentiation, they find that high-frequency stimulation actually makes this nonlinear system operate in a more linear fashion. Although these findings are difficult to incorporate into other data, the power of the technique strongly indicates that such approaches must take an important place in the study of brain changes related to learning and memory.

COMPARATIVE ASPECTS OF LEARNING AND MEMORY

Reviews and discussions of the comparative approach to memory occupy the middle third of the book. Gould describes the remarkable memory of bees for flowers and shows that, among other items, they retain information about odors, colors, shapes, and locations. The question of how relatively simple nervous systems can accomplish all of this leads to the idea that learning consists of changes in the strength of genetically dictated circuitries, suggesting in turn that learning and memory organization need to be analyzed in terms of the innate behavior patterns formed over evolutionary history.

Shettleworth takes up the question of memory for food location in birds. She reviews recent work that convincingly demonstrates an immense capacity and extreme duration of spatial memory and then considers in detail the question of what it is that the birds remember. The all-important comparative issue of how spatial memory in birds relates to that in other animals, and in particular the much studied radial maze learning of rats, is also discussed. Laboratory studies of conditioning in the slug *Limax* are reviewed and discussed by Cooke, Delaney, and Gelperin. The vast body of literature describing conditioning in birds and mammals allows for a quite detailed comparison of this form of learning between different groups, and most notably between vertebrates and invertebrates. One can only be impressed with the many features of Pavlovian conditioning possessed by the slugs, including the apparent necessity for predictability between stimulus

events for conditioning to occur. These points of contact do suggest that the same phenomenon is present across much of the animal kingdom and therefore that deductions about mechanisms arrived at from studies in the invertebrates will have broad applicability. The simple nervous systems of the invertebrates should also be amenable to computer modeling of learning effects and the chapter by Cooke and colleagues describes some recent efforts in this direction. The chapter by Rescorla provides another view of conditioning. For birds and rats, at least, conditioning involves formations of numerous associations other than those that have been concentrated upon in the past. It now seems clear that the animal forms links between stimulus elements, between those elements and the consequents, and between the context and events occurring within it, all during a typical Pavlovian conditioning experiment. Rescorla raises the very significant point that these varieties of learning may follow different rules and therefore that psychological and neurobiological models of associative conditioning are quite possibly greatly oversimplified.

Coss emphasizes evolutionary restraints on learning. He argues that learning may best be viewed as an adjustment of instinct related to variations in ecological niche. Analysis of the antisnake behavior of ground squirrels indicates the retention of information about a specific habitat for thousands of generations. Macphail emphasizes the similarities in learning capacity across phyla, arguing that no species differences have been demonstrated. However, Rosenzweig and Glickman offer a sharply contrasting view. Staddon emphasizes the interplay of selection and variation as determinants of learning. He sees learning as inferences based on two sets of rules: one specific to ecological niche, the other more general.

Overall, these chapters reflect a vital area of rapidly growing interest and attention, the implications of which are critical for neurobiological attempts to understand learning and memory.

LEARNING, MEMORY, AND COGNITIVE PROCESSES

One of the central issues in research on the neurobiology of learning and memory is the question of whether all learning, in humans as well as animals, is based on a single set of principles. This issue is the focus of the chapters in the third section of this book. As the discussions in these chapters indicate, there is currently a growing consensus that there are different forms of learning and memory and that the different forms may be based on different neuronal systems.

At one level, however, the various forms of learning, as seen in various learning tasks, appear to share a common basis. Gallagher presents evidence that treatments affecting endogenous opioid systems have comparable effects in several types of learning tasks in rats. Further, the modulating effects of

opioid hormones on memory seem to work, at least in part, through influences on brain regions—amygdala and hippocampus—and on transmitter systems—adrenergic and cholinergic—that appear, on the basis of evidence from numerous studies, to be involved in information storage in several species.

At another level, however, there appear to be various forms of learning. Mackintosh summarizes evidence showing that animals learn about the relationships among stimuli and that *what* an animal learns when it is trained depends upon the specific way in which information is presented. His view that conditioning consists of acquiring declarative knowledge rather than procedural knowledge contrasts sharply with older as well as some current views that suggest that conditioned response learning consists of learning responses. He also proposes that different forms of learning may involve different neural systems. For example, systems underlying preparatory learning (e.g., affective responses) may differ from those involved in representing the specific information provided by the training stimuli.

This general theme of multiple forms of learning is continued in Schacter's chapter. He argues that, at a descriptive level, some learning and memory is based on explicit recognition and recollection whereas other forms, including skill learning and priming effects, are implicit; that is, they do not depend upon explicit conscious recollection. Further, both memory capacities appear to be intact in amnesic patients. Even though Schacter attempts to remain at a descriptive level, his suggestions and findings immediately raise the question of mechanisms. Do these findings argue that different neuronal systems are involved in these different forms of learning? Further, are forms of memory spared in amnesic patients, based on the same processes? Are there additional forms that have not as yet been identified? Schacter's chapter suggests that there are—or might be.

Schacter's findings and conclusions agree with earlier evidence from studies by Weiskrantz that some form of memory is spared in amnesic patients. As Weiskrantz points out, this evidence argues against the view that amnesics are generally defective in the ability to store new information. Although there is now broad agreement that there is sparing as well as loss of memory in amnesia, there remains disagreement as to whether there is more than one form of amnesia. Weiskrantz argues that there is one core form of the amnesia syndrome and that the memory impairment involves a common neural system.

In contrast, Zola-Morgan and Squire suggest that there is more than one form of amnesia and that different forms are due to damage of different neural structures. Thus, although there is general agreement that memory is spared in amnesic patients, there is, as yet, no consensus concerning the brain regions involved in the memory loss. Further, as Neal Cohen points out, it is not at all clear which structures are responsible for the memory spared in amnesics. This is, of course, an equally important issue. As Crowder emphasizes, the issues of the brain systems involved in declarative and

procedural learning will be difficult to address in view of the evidence summarized by Mackintosh indicating that conditioning procedures seem to engage a declarative system. Finally, Kean argues that there are other grounds for suspecting that it will be difficult to identify the neural structures responsible for different forms of memory loss in amnesics. Any given behavior, she notes, no doubt engages the interaction of many different systems and, thus, any lesion might simply impair memory through disruption of the interactions among the systems. According to this view, it may be premature to identify specific neuronal systems as having specific functions in memories spared and lost in amnesics.

These, then, are the issues addressed in the chapters in the final section of the book. Obviously, attempts to understand the neural basis of learning and memory are enormously complicated by the accumulating evidence that memory may come in many forms. If the many forms are based on different brain systems, the problem is complicated still further. But, the weight of the evidence as well as the thrust of current thinking suggests that it may be unwise to make any simpler assumptions.

REGISTRANTS

Second Conference on the Neurobiology of Learning and Memory

University of California, Irvine

October 6-9, 1984

Dr. Fred Abraham
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Wickliffe C. Abraham
Department of Psychology
University of Otago
Box 56
Dunedin,
New Zealand

Dr. Victor Aleman
Department of Neurosciences
Centro Investigacion de Estudios Avanz.
Apdo. Postal, 14-740 07000
Mexico D.F.

Dr. Ronald Alkana
School of Pharmacy
University of Southern California
1985 Zonal Avenue
Los Angeles, CA 90033

Dr. Daniel L. Alkon
Laboratory of Biophysics
Nat. Inst. of Health at the Marine Bio. Lab.
Woods Hole, MA 02543

Dr. Nahum Allon
Israel Institute of Biological Research
P.O. Box 19
Ness-Ziona,
Israel,70450

Dr. Harvey J. Altman
Department of Geriatrics
Lafayette Clinic
951 E. Lafayette
Detroit, MI 48207

Dr. Kenneth Z. Altshuler
Department of Psychiatry
Univ. of Tex. Health Sci. Center
5323 Harry Hines
Dallas, Texas 75235

Dr. David G. Amaral
Developmental Neurobiology
Salk Institute
P.O. Box 85800
San Diego, CA 92138

Ms. Denise Arst
Department of Psychiatry
University of Pittsburgh
Pittsburgh, PA 15261

Ms. Deborah Arthur
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. John H. Ashe
Department of Psychology
University of California
Riverside, CA 92521

Dr. Dana Aswad
Department of Psychobiology
University of California, Irvine
Irvine, CA 92717

Dr. Carlos Avendano
Developmental Neurobiology
The Salk Institute
P.O. Box 85800
San Diego, CA 85800

Dr. Jocelyne Bachevalier
Lab. Neuropsychology
NIMH
9000 Rockville Pike, Bldg. 9, Rm. 1N107
Bethesda, MD 20205

Mr. Stephen Back
Department of Pharmacology
University of California
Irvine, CA 92717

Dr. Isaac Bakst
Developmental Neurobiology
Salk Institute
P.O. Box 85800
San Diego, CA 92138

Mr. Barry Bank
Div. of Life Sciences
University of Toronto
Scarborough College, W. Hill
Toronto, Ontario MICIA4
Canada

Dr. Carol Barnes
Department of Psychology
University of Colorado
Box 345
Boulder, CO 80309

Dr. German A. Barrionuevo
Division of Neurosciences
Beckman Research Inst. of City of Hope
1450 East Duarte Road
Duarte, CA 91010

Dr. Jennifer Barron
Department of Psychology
Fairview Hospital
2501 Harbor Blvd.
Costa Mesa, CA 92626

Ms. Julia L. Bassett
Psychobiology Program
University of Pittsburgh
461 C Crawford Hall
Pittsburgh, PA 15260

Dr. Michel Baudry
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. William W. Beatty
Department of Psychology
North Dakota State University
Fargo, ND 58105

Dr. James D. Bellu[illegible]zi
Department of Pharmacology
University of California
Irvine, CA 92717

Mr. David Benjamin
Information and Computer Science
University of California
Irvine, CA 92717

Ms. Susan Benloucif
Department of Psychology
University of California
Tolman Hall
Berkeley, CA 94720

Dr. Cathy Bennett
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Theodore W. Berger
Department of Psychology
University of Pittsburgh
495 Crawford Hall
Pittsburgh, PA 15260

Dr. Robert F. Berman
Department of Psychology
Wayne State University
71 W. Warren
Detroit, MI 48202

Dr. Federico Bermudez-Rattoni
Department of Psychology
University of California
760 Westwood Plaza, Rm 58-228
Los Angeles, CA 90024

Dr. Niles Bernick
National Institute of Mental Health
Neuroscience Research Branch
5600 Fishers Lane, Room 10C09
Rockville, MD 20857

Dr. Stephen D. Berry
Department of Psychology
Miami University
112 Benton Hall
Oxford, OH 45056

Dr. William O. Berry
Directorate of Life Sciences
Air Force Office of Scientific Research
Bolling Air Force Base
Washington D.C., 20332

Dr. Phillip Best
Department of Psychology
University of Virginia
Gilmer Hall
Charlottesville, VA 22901

Mr. Joel Black
Department of Pharmacology
University of California
Irvine, CA 92717

Mr. James Blackburn
Department of Psychology
University of British Columbia
2136 West Mall
Vancouver, Br. Columbia V6T 1Y7
Canada

Ms. Elizabeth Bostock
Department of Neurobiology
University of North Carolina
118 Davie Hall 013A
Chapel Hill, NC 27514

Dr. Sarah W. Bottjer
Department of Psychology
University of California
Los Angeles, CA 90024

Dr. Richard Bridges
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Kenneth Brown
Department of Psychiatry
University of California, San Diego
La Jolla, CA 92093

Dr. Michael D. Browning
Cellular and Molecular Neuroscience
Rockefeller University
1230 York Avenue
New York, NY 10021

Ms. Marsha Bundman
Department of Pharmacology
University of California
357 Med Surge II
Irvine, CA 92717

Dr. William E. Bunney
Department of Psychiatry
University of California
Irvine, CA 92717

Mr. Michael Buttrick
Department of Psychology
University of British Columbia
4217 W. 14th Avenue
Vancouver, Br. Columbia V6R 2X7
Canada

Mr. Lawrence F. Cahill
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Kenneth A. Campbell
Department of Physiology
Bowman Gray School of Medicine
300 S. Hawthorne Road
Winston-Salem, NC 27103

Mr. James Canfield
1421 Liberty St. No. 6
El Cerrito, CA 94530

Dr. Rene Carmona
Department of Mathematics
University of California
Irvine, CA 92717

Dr. James E. Carnahan
Central Research Department
Dupont Experimental Station
Wilmington, DE 19898

Ms. Melissa Carpenter
Department of Psychobiology
University of California
Irvine, CA 92717

Mr. Eduardo C. Cascallar
1222 Oak Street
So. Pasadena, CA 91030

Dr. J. M. Cassady
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Ms. Claudia Castle
11931 S. Oak Glen Road
Yucaipa, CA 92399

Dr. Mary L. Castle
280 La Colina Dr.
Redlands, CA 92373

Ms. Adele R. Chandler
Counseling Department
Grossmont Community College
8800 Grossmont College Dr.
El Cajon, CA 92020

Dr. Greg R. Christoph
Central Research Department
Dupont Experimental Station
Wilmington, DE 19898

Dr. Gregory A. Clark
Center for Neurobiology and Behavior
Columbia Univerasity
722 W. 168th St.
New York, NY 10032

Dr. David H. Cohen
Neurobiology and Behavior
State University of New York
Stony Brook, NY 11794

Dr. Neal J. Cohen
Dept. of Psychology and Neurology
Johns Hopkins University
330G Ames Hall
Baltimore, MD 21218

Dr. Ruth M. Colwill
Center for Neurobiology and Behavior
Columbia University
722 W. 68th St.
New York, New York 10032

Mr. Peter H. Cooper
Department of Psychology
University of California
Los Angeles, CA 90024

Dr. Catherine Cornwell-Jones
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Richard G. Coss
Department of Psychology
University of California
Davis, CA 95616

Dr. Francis Crick
The Salk Institute
10010 N. Torrey Pines Rd.
La Jolla, CA 92037

Dr. Robert G. Crowder
Department of Psychology
Yale University
Box 11A, Yale Station
New Haven, CT 06520

Dr. Peter Curzon
Department of Biology
Searle Labs/Div. of GD Searle
4901 Searle Parkway
Skokie, IL 60077

Dr. Joel L. Davis
Aging and Behavioral Biology Research
VA Medical Center
16111 Plummer Street
Sepulveda, CA 91343

Dr. Samuel A. Deadwyler
Department of Physiology and Pharmacology
Bowman Gray School of Medicine
300 S. Hawthorne
Winston Salem, NC 27103

Dr. Claude Destrade
Dept. of Psychophysiologie
University Bordeaux I
Avenue des Facultes
33405 Talence, Cedex
France

Mr. David Diamond
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Malcolm B. Dick
School of Social Science
University of California
Irvine, CA 92717

Dr. R. K. Dismukes
Air Force Office of Scientific Research
Bolling Air Force Base
Washington, D.C. 20332

Dr. Nelson Donegan
Department of Psychology
Stanford University
Bldg 420, Jordan Hall
Stanford, CA 94305

Mr. Jonathan Druhan
Department of Psychology
University of British Columbia
2136 West Mall
Vancouver, Br. Columbia V6T 1Y7
Canada

Dr. David Easton
Social Sciences
University of California
Irvine, CA 92717

Dr. Hugh L. Evans
Environmental Medicine
NYU Medical Center
P.O. Box 817
Tuxedo Park, NY 10987

Mr. Laurent Fagni
Physiologie Hyperbare
C.N.R.S.
Fac. de Medecine Nord. Bd. Pierre-Dramard
13015 Marseille,
France

Dr. Richard J. Fanelli
Department of Psychology
University of North Carolina
Davie Hall 013A
Chapel Hill, NC 27514

Mr. Robert Finn
9040 Cris Avenue, Apt. 7
Anaheim, CA 92804

Dr. William Fishbein
Department of Psychology
City College New York
138th Street and Convent Ave.
New York, NY 10031

Dr. Hans Flohr
Department of Neurobiology
University of Bremen
2800 Breman 33,
Fed Rep Germ

Dr. Robin Forman
Laboratory of Biophysics, NINCDS
National Institutes of Health
Marine Biological Laboratory
Woods Hole, MA 02543

Dr. Joaquin M. Fuster
Department of Psychiatry
UCLA Medical Center
760 Westwood Plaza
Los Angeles, CA 90024

Dr. Michael Gabriel
Department of Psychology
University of Illinois
603 E. Daniel St.
Champaign, IL 61820

Dr. Christine Gall
Department of Anatomy
University of California
Irvine, CA 92717

Dr. Michela Gallagher
Department of Psychology
University of North Carolina
Davie Hall 013A
Chapel Hill, NC 27514

Dr. Elkan Gamzu
Department of Pharmacology I
Hoffmann-La Roche
340 Kingsland Street
Nutley, NJ 07110

Mr. Alan Ganong
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Jim Geddes
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Alan Gelperin
Molecular Biophysics
AT&T Bell Laboratories
600 Mountain Avenue
Murray Hill, NJ 07974

Dr. Harry Geyer
Department of Pharmacology
HOECHST-ROUSSEL Pharmaceuticals, Inc.
Route 202-206 North
Somerville, NJ 08876

Mr. Robert Gibbs
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Graham V. Goddard
Department of Psychology
University of Otago
Box 56
Dunedin,
New Zealand

Dr. Paul E. Gold
Department of Psychology
University of Virginia
Gilmer Hall
Charlottesville, VA 22901

Dr. Louis A. Gottschalk
Psychiatry and Human Behavior
University of California
Irvine, CA 92717

Dr. James L. Gould
Department of Biology
Princeton University
Princeton, NJ 08544

Dr. Richard H. Granger
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Ms. Susan Graves
The Irvine Company
550 C Newport Center Drive
Newport Beach, CA 92658

Dr. William T. Greenough
Department of Psychology
University of Illinois
603 E. Daniel
Champaign, IL 61820

Mr. Steven M. Guich
Social Sciences/Dept. of Medicine
University of California
Irvine, CA 92717

Dr. Henry J. Haigler
Department of Biology
G.D. Searle & Co./Searle Labs
4901 Searle Parkway
Skokie, IL 60077

Ms. Shelley Halpain
Rockefeller University
1230 York Avenue
New York, NY 10021

Mr. Mark Hammer
Department of Psychology
University of Alberta
Edmonton, Alberta T6H 2B9
Canada

Mr. Steven Hampson
Information and Computer Science
University of California
Irvine, CA 92717

Dr. Eric W. Harris
Department of Psychobiology
University of California
Irvine, CA 92717

Ms. Melinda Hauser
Developmental & Cell Biology
University of California
Irvine, CA 92717

Dr. John Haycock
Lab. Cellular & Molecular Neurosci.
Rockefeller University
1230 York Ave.
New York, NY 10021

Mr. Howard N. Henry
Information & Computer Science
University of California
Irvine, CA 92717

Ms. Arlene Hirano
Department of Neurobiology
The Rockefeller University
1230 York Ave.
New York, NY 10021

Dr. Franz Hock
Pharmacology H 821
HOECHST AG
Postfach 80 03 20 D-6230
Frankfurt, M.80
Fed Rep Germ

Mr. Robert N. Holdefer
Department of Psychology
Southern Illinois University
Carbondale, IL 62901

Mr. Lawrence Howard
Social Sciences
University of California
Irvine, CA 92717

Dr. Donna Huey
Department of Psychology
John Hopkins University
Baltimore, MD 21218

Ms. Carol A. Hunt
Department of Anatomy
University of California
Irvine, CA 92717

Dr. Joseph P. Huston
Institute of Psychology
University of Dusseldorf
Universitatsstrasse 1
Dusseldorf, 4000
Fed Rep Germ

Dr. Donald K. Ingram
Gerontology Research Center
Francis Scott Key Medical Center
Baltimore, MD 21224

Dr. Ines Introini
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Ms. Krystyna Isaacs
1156 N. Moore Road
Camano Island, WA 98292

Dr. Gwen Ivy
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Ivan Izquierdo
Department of Bioquimica
Inst. Biociencias
UFRGS (centro) 90.000
Porto Alegre, RS
Brazil

Dr. William J. Jacobs
Department of Psychology
University of British Columbia
2075 Wesbrook Mall
Vancouver, Brt. Columbia V6T 1W5
Canada

Dr. Robert Jaffard
Lab Psychophysiologie
Universite Bordeaux Iz I
Avenue des Facultes 33405
Talence Cedex,
France

Dr. Murray E. Jarvik
Psychiatry and Pharmacology
University of California
VA Medical Center
Los Angeles, CA 90073

Dr. John GR Jefferys
Department of Neurophysiology
Institute of Neurology
Queens Square
London, WC1 N3BG
England

Mr. John Jensen
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Robert A. Jensen
Department of Psychology
Southern Illinois University
Carbondale, IL 62901

Dr. Robert K. Josephson
Department of Psychobiology
University of California
Irvine, CA 92717

Mr. David A. Kaufman
Department of Neuroscience
University of Pennsylvania
School of Medicine
Philadelphia, PA 19104

Dr. Mary-Louise Kean
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Stephen R. Kelso
Division of Neuroscience
Beckman Research Institute
1450 E. Duarte Road
Duarte, CA 91010

Mr. Duncan Kennedy
Department of Psychology
University of British Columbia
3336 W12th Ave.
Vancouver, Br. Columbia V6R 2M9
Canada

Dr. Patrick Kesslak
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Markus Kessler
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Leonard M. Kitzes
Department of Anatomy
University of California
Irvine, CA 92717

Ms. Barbara Knowlton
Department of Psychology
Stanford University
Crothers Hall
Stanford, CA 94305

Dr. Harold Koopowitz
Developmental and Cell Biology
University of California
Irvine, CA 92717

Ms. Lynn Kooyman
Department of Psychology-Physiology
University of California
Riverside, CA 92521

Ms. Donna Korol
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Danuta M. Kowalska
Laboratory of Neuropsychology
National Institute of Mental Health
9000 Rockville Pike
Bethesda, MD 20205

Ms. Kathy Kramer
Department of Psychobiology
University of California
Irvine, CA 92717

Ms. Elizabeth M. Kurz
Cognitive Sciences
University of California
Irvine, CA 92717

Dr. David LaBerge
Cognitive Sciences
University of California
Irvine, CA 92717

Dr. Philip W. Landfield
Department of Physiology and Pharmacology
Bowman Gray School of Medicine
300 S. Hawthorne
Winston-Salem, NC 27103

Mr. John Larson
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Joseph LeDoux
Department of Neurology
Cornell University Medical College
411 E. 69th Street
New York, NY 10021

Dr. Nancy J. Leith
CNS Pharmacology
G.D. Searle
4901 Searle Parkway
Skokie, IL 60077

Mr. Robert Lennartz
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Michael Leon
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Barbara Lerer
Biomedical Products Department
Dupont Company
Experimental Station 400/4422
Wilmington, DE 19898

Dr. Frances Leslie
Department of Pharmacology
University of California
Med Surge II, Rm. 360
Irvine, CA 92717

Mr. David Levine
Department of Psychobiology
University of California
Irvine, CA 92717

Mr. Richard S. Lewis
Department of Psychology
Michigan State University
East Lansing, MI 48840

Dr. Keng Chen Liang
Department of Psychology
National Taiwan University
Taipei, Taiwan
R.O.C. 107

Ms. Christine Lofgren
Cognitive Science
University of California
Irvine, CA 92717

Dr. Sandra E. Loughlin
Department of Pharmacology
University of California
Irvine, CA 92717

Dr. Richard H. Lovely
Neurosciences Group, Biology Dept.
Battelle-Northwest
Richland, WA 99352

Dr. Gary Lynch
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Ms. Melody MacDonald
16261 Sierra Street
Fountain Valley, CA 92708

Dr. N. J. Mackintosh
Department of Experimental Psychology
University of Cambridge
Downing Street
Cambridge,
England

Dr. Euan Macphail
Department of Psychology
University of York
York,
England

Dr. John Madden
Psychiatry & Behavioral Sciences
Stanford University
Stanford, CA 94305

Ms. Laura A. Mamounas
Department of Neurophysiology
University of Wisconsin
627 Waisman Center 420
Madison, Wisconsin 53706

Dr. James L. McGaugh
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Terry R. McGuire
Dept. of Bio. Sci.
Rutgers University
Piscataway, NJ 08854

Dr. Thomas M. McKenna
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Bruce L. McNaughton
Department of Psychology
University of Colorado
Campus Box 345
Boulder, CO 80309

Mr. Dale McNulty
Information & Computer Science
University of California
Irvine, CA 92717

Dr. Leslie McPherson
Department of Psychology
University of British Columbia
P.O. Box 46497, Station G
Vancouver, BC V6R4G7

Ms. Pat Merjanian
Cognitive Sciences
University of California
Irvine, CA 92717

Dr. Rita B. Messing
Department of Pharmacology
University of Minnesota
3-260 Millard Hall
Minneapolis, MN 55455

Dr. Henry J. Michalewski
Department of Neurology
University of California
Med Surg I, Room 150
Irvine, CA 92717

Dr. Ricardo Miledi
Department of Psychobiology
University of California
Irvine, CA 92717

Ms. Sheri Mizumori
Department of Psychology
University of California
3210 Tolman Hall
Berkeley, CA 94720

Mr. Daniel T. Monaghan
Department of Psychobiology
University of California
Irvine, CA 92717

Mr. James S. Morgan
Systems Engineering Division
Systems and Applied Sciences Corp.
1020 Woodman Drive
Dayton, Ohio 45432

Mr. Anthony Morielli
Thimann Labs
University of California
Santa Cruz, CA 95064

Dr. Richard GM Morris
MRC Cognitive Neuroscience Group
University of St. Andrews
United Kingdom

Dr. Sarah Mosko
Department of Neurology
University of California, Irvine, Med. Ctr.
101 City Drive South
Orange, CA 92668

Dr. Lynn Nadel
Social Sciences
University of California
Irvine, CA 92717

Dr. Gary Novack
Allergan Pharmaceuticals
2525 Dupont Dr.
Irvine, CA 92713

Dr. Thomas A. O'Connor
Department of Neurology
University of California
151 Med Surge I
Irvine, CA 92717

Dr. Lynn C. Oatman
Behavioral Research
U.S. Army Human Eng. Lab
135 Black Oak Drive
Elkton, MD 21921

Dr. Michael Oliver
Department of Physiology
University of British Columbia
2146 Health Sciences Mall
Vancouver, Br. Columbia V6T 1W5
Canada

Dr. Kathie Olsen
Psychobiology Program
National Science Foundation
1800 G. St., N.W.
Washington, DC 20008

Dr. David S. Olton
Department of Psychology
Johns Hopkins University
Charles & 34th Streets
Baltimore, MD 21218

Dr. Alejandro Oscos
Department of Neurosciences
Centro de Investigacion y Est. Avanzados
Apdo. Postal, 14-740 07000
Mexico D.F.

Dr. Tilmann Ott
Pharmacology and Toxicology
Humboldt University Berlin
1080 Berlin
Germ Dem Rep

Mr. Ken Paller
Department of Neurosciences, M-008
University of California, San Diego
La Jolla, CA 92093

Ms. Beatrice Passani
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Michael M. Patterson
College of Osteopathic Medicine
Ohio University
Richland Avenue
Athens, OH 45701

Ms. Teresa A. Patterson
Department of Psychology
University of California
Berkeley, CA 94720

Dr. Donald H. Perkel
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Lynn Perlmutter
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Rita W. Peterson
Office of Teacher Education
University of California
Irvine, CA 92717

Mr. James G. Pfaus
Department of Psychology
University of British Columbia
2136 West Mall
Vancouver, Br. Columbia V6T 1Y7
Canada

Dr. Robert Pfeffer
Department of Neurology
Univ. of Calif., Irvine, Med. Ctr.
Orange, CA 92668

Dr. Anthony G. Phillips
Department of Psychology
University of British Columbia
2075 Wesbrook Cres.
Vancouver, Br. Columbia V6T 1W5
Canada

Dr. Richard M. Pico
Department of Anatomy
University of California
Irvine, CA 92717

Mr. Jaime A. Pineda
Neuroscience Department M008
University of California, San Diego
La Jolla, CA 92037

Dr. Sarah Pixley
Department of Psychobiology
University of California
Irvine, CA 92717

Dr. Mu-ming Poo
Physiology and Biophysics
University of California
Irvine, CA 92717

Ms. Isabelle R. Poston
Department of Psychology
University of California, Irvine
Irvine, CA 92717

Ms. Patricia Potter
6 Ruby Ridge Road
Anniston, AL 36202

Ms. Shannon Powers
California College of Medicine
University of California
Irvine, CA 92717

Mr. Peter Rapp
Department of Psychology
University of North Carolina
Davie Hall 013A
Chapel Hill, NC 27514

Dr. Robert Rescorla
Department of Psychology
University of Pennsylvania
3815 Walnut Street
Philadelphia, PA 19104

Dr. Charles E. Ribak
Department of Anatomy
University of California
Med Surge II, Room 364
Irvine, CA 92717

Ms. Joyce P. Riley
Orange County Chapter
CANHC-ACLD
406 E. Bay St.
Costa Mesa, CA 92627

Dr. Patricia Rinaldi
Department of Neurosurgery
University of California
Irvine, CA 92717

Dr. Gregory M. Rose
Department of Pharmacology
University of Colorado Health Sci. Ctr.
Box C236, 4200 E. 9th Street
Denver, CO 80262

Dr. Carl Rosenberg
Department of Neurology
Univ. of Calif., Irvine, Med. Ctr.
Orange, CA 92668

Dr. Mark R. Rosenzweig
Department of Psychology
University of California
Tolman Hall
Berkeley, CA 94720

Dr. Tsunao Saitoh
Center for Neurobiology and Behavior
Columbia University
722 West 168th Street
New York, NY 10032

Dr. Curt Sandman
Department of Psychiatry
Univ. of Calif., Irvine, Med. Ctr.
101 City Drive South
Orange, CA 92668

Dr. John M. Sarvey
Department of Pharmacology
Uniformed Serv. Univ. of Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814

Dr. Daniel Schacter
Department of Psychology
University of Toronto
100 St. George St.
Toronto, Ontario M55 1A1
Canada

Ms. Helen Scharfman
Department of Pharmacology
Uniformed Serv. Univ. of Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814

Mr. Jeffrey C. Schlimmer
Information and Computer Science
University of California
Irvine, CA 92717

Mr. Frank Schottler
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Laszlo Seress
Department of Physiology
University Medical School
Pecs, Szigetti M-17
Hungary

Mr. Kim B. Seroogy
Department of Anatomy
University of California
Irvine, CA 92717

Mr. Matthew L. Shapiro
Department of Psychology
Johns Hopkins University
3400 North Charles St.
Baltimore, MD 21218

Dr. Gordon Shaw
Department of Physics
University of California
Irvine, CA 92717

Dr. David F. Sherry
Department of Psychology
University of Toronto
Toronto, Ontario M5S 1A1
Canada

Dr. Sara Shettleworth
Department of Psychology
University of Toronto
Toronto, Ontario MSS 1A1
Canada

Dr. Arthur Shimamura
VA Medical Center, V-116A
3350 La Jolla Village Drive
San Diego, CA 92161

Dr. Zhang Shi-Yi
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Mr. Richard Shrum
Thimann Labs
University of California
Santa Cruz, CA 95064

Dr. Dennis Silverman
Department of Physics
University of California
Irvine, CA 92717

Dr. Robert Siman
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Ronald W. Skelton
Department of Psychology
University of Victoria
Box 1700
Victoria, Br. Columbia V8W 3Y2
Canada

Dr. Curtis G. Smith
Department of Biology
Mount Holyoke College
South Hadley, MA 01075

Dr. Larry R. Squire
Department of Psychiatry
University of California, San Diego
La Jolla, CA 92161

Dr. John Staddon
Department of Psychology
Duke University
Durham, NC 27706

Dr. Thomas A. Standish
Information and Computer Science
University of California
Irvine, CA 92717

Dr. Mark E. Stanton
Department of Psychiatry & Behav. Sciences
Stanford University School of Medicine
Stanford, CA 94305

Mr. Patric K. Stanton
Department of Pharmacology
Uniformed Serv. Univ. of Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814

Dr. Arnold Starr
Department of Neurology
University of California
Irvine, CA 92717

Dr. Ursula Staubli
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Larry Stein
Department of Pharmacology
University of California
Irvine, CA 92717

Dr. Debra B. Sternberg
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Michael G. Stewart
Department of Biology
The Open University
Milton Keynes
Milton Keynes, MK7 GAA
England

Dr. James M. Swanson
Department of Psychiatry
University of California
Irvine, CA 92717

Dr. Timothy J. Teyler
Neurobiology Program
Northeastern Ohio University
Rootstown, OH 44272

Lucian Thompson
Department of Psychology
University of Virginia
Gilmer Hall
Charlottesville, VA 22901

Dr. Richard F. Thompson
Department of Psychology
Stanford University
Palo Alto, CA 94305

Dr. Robert Thompson
Physical Medicine & Rehabilitation
Univ. of Calif., Irvine, Med. Ctr.
Route 81
Orange, CA 92668

Dr. Jerome Tobis
Physical Medicine and Rehabilitation
Univ. of Calif., Irvine, Med. Ctr.
Orange, CA 92668

Mr. Keith Trujillo
Department of Pharmacology
University of California
Irvine, CA 92717

Ms. Cyma van Petten
Department of Neurosciences
Univ. of Calif., San Diego
N-008
La Jolla, CA 92093

Dr. Beatriz Vasquez
Department of Pharmacology
Research Service 151 VA Hospital
11201 Benton St.
Loma Linda, CA 92357

Dr. David M. Warburton
Department of Psychology
The University of Reading
Reading, RG6 2AH
England

Dr. Norman M. Weinberger
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Dr. Lawrence Weiskrantz
Department of Experimental Psychology
University of Oxford
South Parks Road
Oxford, OX1 3UD
England

Dr. Gary L. Wenk
Department of Psychology
Johns Hopkins University
34th and Charles Street
Baltimore, MD 21218

Dr. Jurgen Wenzel
Anatomisches Institute
Humboldt Universitat
Philippstrasse 12
1040 Berlin,
Germ Dem Rep

Dr. K. Wesnes
Department of Psychology
University of Reading
Reading, RG6 2AL
England

Dr. Kenneth Wexler
School of Social Sciences
University of California
Irvine, CA 92717

Ms. Cynthia G. Wible
Psychology Department
Johns Hopkins University
Ames Hall
Baltimore, MD 21218

Dr. Jeffrey Willner
School of Social Sciences
University of California
Irvine, CA 92717

Dr. Don Wilson
Ctr. for Neurobio. of Learning & Memory
University of California
Irvine, CA 92717

Mr. Marty Woldorff
Department of Neurosciences
Univ. of Calif., San Diego
N-008
La Jolla, CA 92093

Ms. Cynthia Woo
Department of Psychobiology
University of California
Irvine, CA 92717

Mr. William G. Wright
Biological Oceanography
Scripps Institute of Oceanography
University of California
San Diego, CA 92093

Dr. Joseph Wu
Department of Psychiatry
University of California
Irvine, CA 92717

Ms. Cherylon Yarosh
Department of Psychology
University of California
Riverside, CA 92521

Mr. Michal Young
Information and Computer Science
University of California
Irvine, CA 92717

Dr. Steven H. Young
Physiology and Biophysics
University of California
D340 Med. Sci. I
Irvine, CA 92717

Dr. Jen Yu
Physical Medicine & Rehabilitation
Univ. of Calif., Irvine, Med. Ctr.
101 The City Dr.
Orange, CA 92668

Dr. Stuart Zola-Morgan
Department of Psychiatry
University of California, San Diego
La Jolla, CA 92093

Dr. Steven F. Zornetzer
Office of Naval Research
800 N. Quincy Street
Arlington, VA 22217

Ms. Joyce Zouzounis
Department of Psychiatry
University of California, San Diego
La Jolla, CA 92093

END

DTIC

8-86